VOLUME 34 APRIL 1941 NUMBER 4

Southern Medical Journal

Journal of the Southern Medical Association

Copyright, Southern Medical Association, 1941. Published monthly by the Southern Medical Association, Empire Building, Birmingham, Alabama. Annual subscription, $4.00. Entered as Second Class Matter at the Post Office at Birmingham, Alabama, under Act of March 3, 1879. Acceptance for mailing at special rate of postage provided for in Section 1103, Act of October 3, 1917, authorized December 20, 1921.

Southern Medical Association, Thirty-Fifth Annual Meeting, St. Louis, Missouri, November 11-14

TABLE OF CONTENTS

Body Section Radiography in the Diagnosis of Aortic Aneurysms and Mediastinal Tumors. Wendell G. Scott, Sherwood Moore and Thomas G. Russell, St. Louis, Missouri 343

Discussed by E. L. Shiflett, Louisville, Ky.; Thomas H. Lipscomb, Jacksonville, Fla.

Hiatus Hernia of the Stomach: Incidence, Symptoms and Medical Management in 1,220 Gastro-Intestinal Cases. Moise D. Levy and L. B. Duggan, Houston, Texas 351

A Clinicopathologic Discussion of Hyperplastic Lesions of the Urinary Tract. W. Calhoun Stirling and J. E. Ash, Washington, D. C. 358

Discussed by Jefferson C. Pennington, Nashville, Tenn.; T. Leon Howard, Denver, Col.; Harry M. Spence, Dallas, Tex.; C. P. Segard, Leonia, N. J.

Epidermolysis Bullosa Acquisita. Joseph L. Hundley and Dudley C. Smith, Charlottesville, Virginia 364

Discussed by Everett S. Lain, Oklahoma City, Okla.; Andrew L. Glaze, Birmingham, Ala.; Robert Brandt, Augusta, Ga.

Car Window Elbows. Howard B. Shorbe, Oklahoma City, Oklahoma 372

Discussed by Hugh Smith, Memphis, Tenn.; Charles F. Wood, Louisville, Ky.

The Pathogenicity of Strains of Brucella Obtained from Cases of Hodgkin's Disease. Wiley D. Forbus and J. U. Gunter, Durham, North Carolina 376

Discussed by George T. Caldwell, Dallas, Tex.; M. Pinson Neal, Columbia, Mo.; Elizabeth Gambrell, Emory University, Ga.; Roy R. Kracke, Emory University, Ga.; Oscar B. Hunter, Washington, D. C.

Neural Myatrophy and Vitamin E. W. de Gutierrez-Mahoney, Nashville, Tennessee 389

Discussed by Seale Harris, Birmingham, Ala.; W. B. Bean, Cincinnati, O.

The Use of Liver Extract in Lupus Erythematosus: A Preliminary Report. Howard King and C. M. Hamilton, Nashville, Tennessee 394

Discussed by Toulmin Gaines, Mobile, Ala.; E. S. Lain, Oklahoma City, Okla.

Common Nutritional Fallacies. William Weston, Columbia, South Carolina 397

Discussed by J. K. Mack, Louisville, Ky.; Seale Harris, Birmingham, Ala.

Operation for Relief of Ascites in Hepatic Cirrhosis. Thomas O. Otto, Miami, Florida 401

Discussed by H. Hart Hagan, Louisville, Ky.; Guy Aud, Louisville, Ky.; J. M. Frehling, Louisville, Ky.; L. Wallace Frank, Louisville, Ky.

Uterine Bleeding from the Viewpoint of the Obstetrician. Nicholson J. Eastman, Baltimore, Maryland 405

Genital Bleeding from the Gynecologist's Viewpoint. Richard W. TeLinde, Baltimore, Maryland 408

Continued on Next Page

TABLE OF CONTENTS—Continued

Endocrinopathic Uterine Bleeding. Emil Novak, Baltimore, Maryland ... 410

Symposium on Uterine Bleeding, Papers of Dr. Eastman, Dr. TeLinde and Dr. Novak, discussed by F. M. Massie, Lexington, Ky.; J. W. Kelso, Oklahoma City, Okla.; Gilbert F. Douglas, Birmingham, Ala.; Misch Casper, Louisville, Ky.

Gastro-Intestinal Allergy: Its Present Status. Albert F. R. Andresen, Brooklyn, New York ... 418

Discussed by Warren T. Vaughan, Richmond, Va.; Seale Harris, Birmingham, Ala.; Morris Shushan, New Orleans, La.

Recurrent Erosions of the Cornea. Maxwell Thomas, Dallas, Texas ... 426

Discussed by J. Wesley McKinney, Memphis, Tenn.; F. B. Blackmar, Columbus, Ga.; W. M. James, St. Louis, Mo.

Further Observations on the Pathogenesis and Localization of Pulmonary Tuberculosis. Benjamin L. Brock, Waverly Hills, Kentucky ... 434

Ten Years in Maternity and Infancy Work in North Carolina. George M. Cooper, Raleigh, North Carolina ... 437

Discussed by R. W. Ball, Columbia, S. C.; J. H. M. Knox, Baltimore, Md.

Results of Abdominal Stabilizations. George O. Eaton, Baltimore, Maryland ... 443

Discussed by Charles E. Irwin, Warm Springs, Ga.; Lenox D. Baker, Durham, N. C.

EDITORIALS ... 446

Drugs for Pneumonia
Muscle Degeneration After Nerve Injury
Hysterectomy and the Ovaries
Twenty-Five Years Ago

BOOK REVIEWS ... 449

SOUTHERN MEDICAL NEWS ... 452

Cecil's MEDICINE

Cecil's "Medicine" has just been thoroughly revised from title to index. **10 entirely new articles** have been added, **30 other contributions completely rewritten,** and every page subjected to the closest scrutiny to make certain that the entire book reflects the most recent developments in today's practice. More than that, 131 additional illustrations have been included.

Among the new and rewritten subjects you will find those on chronic bromide poisoning, riboflavin deficiency, uveoparotid fever, regional ileitis, herpes zoster, mumps, gonococcus infection, tuberculosis, malaria, gout and gouty arthritis, diseases of the stomach, gallbladder, bile ducts, lungs, kidneys, arteries, bones, glands, etc.

Causes, symptoms, tests, diagnostic methods—all are covered in concise but full detail. On treatment you will find particular stress. You are given the newest in drugs, serums, vaccines and other agents and told exactly when and how to use them in treating your own patients.

TEXTBOOK OF MEDICINE. By 144 American Authorities. Edited by RUSSELL L. CECIL, M.D., Professor of Clinical Medicine, Cornell University Medical College. Octavo of 1744 pages, illustrated. Cloth, $9.50

New (5th) Edition—Published August, 1940.

Send Orders to

J. A. MAJORS COMPANY

New Orleans **Dallas**

Critics Acclaim KEY *and* CONWELL'S

FRACTURES, DISLOCATIONS AND SPRAINS

By JOHN ALBERT KEY and H. EARLE CONWELL
2nd Edition. 1246 pages, 1224 illustrations
PRICE, $12.50

Pronounced by critics everywhere the "best" in its field, this volume is one which every surgeon should have at hand at all times. The authors cover the management of fractures, dislocations and sprains completely, presenting practical, tested methods by means of clear, simple discussion and excellent illustrations.

The book considers the Etiology, Symptoms, Diagnosis, Management, Handling of Complications, Transportation of Fracture Patients, First Aid in Fractures and Auto Injuries, and Workmen's Compensation Law Affecting Fracture Cases and Medico-Legal Aspects of Fracture Cases. Each chapter on regional fractures and dislocations is preceded by a well-illustrated discussion of the surgical anatomy. Principles and choice of treatment are given rather than the outlining of one method alone, and all apparatus for traction, splinting, bracing, etc., is well demonstrated. Take advantage of the help this volume can give you. Send for your copy today!

- "This book is one of the best and most complete, as well as concise descriptions of the principles, general aspects, diagnosis and treatment of specific injuries of the skeletal system that one could desire." —**Minnesota Medicine.**
- "There is no better test for the merits of a book than referring to it on the spur of the moment when certain problem cases appear in one's daily practice; such a test has been made, and this book found very satisfactory."—**Hahnemannian Monthly.**
- "This book seems complete and up to date in every detail. One can not recommend it too highly to anyone interested in fractures, dislocations or sprains, as all methods described are sound and have been thoroughly tested out."—**Southwestern Medicine.**
- "Every physician, regardless of his specialty, should read such a chapter as that on 'First Aid in Fractures and Automobile Injuries'."—**Detroit Medical News.**
- "To the average individual one illustration is worth several pages of descriptive matter, and a great many of the fractures discussed are so pictorially portrayed that very little discussion is necessary." —**Journal of the Iowa State Medical Society.**
- "All the modern methods of treatment in general use, from the simplest to the most elaborate, are carefully described so that everyone, from the country doctor to the specializing orthopedist in the city hospital, will find what he needs to know from the skull to the metatarsal bones, all arranged in orderly sequence."—**Clinical Medicine and Surgery.**

CLINICAL PELLAGRA

Written by a man who has been a student of pellagra for 34 years, this book takes up all phases of pellagra. First History, the results of past investigations and recent developments are given and correlated and then diagnosis, prevention and treatment are thoroughly discussed.

By Seale Harris and Seale Harris, Jr. 494 pages, 66 illustrations. Price, $7.00.

PRINCIPLES of SURGICAL CARE

This new text emphasizes the fact that making the patient safe for the operation is as important as making the operation safe for the patient. The author deals with principles which he himself has tested and found sound, and covers not only shock but other disorders as well.

By Alfred Blalock. 309 pages, 13 illustrations. Price, $4.50.

The C. V. Mosby Company SMJ 4-41
3525 Pine Blvd., St. Louis, Mo.

Gentlemen: Send me the following book(s).....

.....

( ) Attached is my check ( ) Charge my account

Dr.....

Address.....

A GOOD "DRINKING" MILK

"The data obtained on the effect of evaporated milk on mineral and nitrogen metabolism in these average healthy children [from 4½ to 6 years of age] are in accordance with those obtained in studies with infants. . . . The main objection to this milk product, unpalatability, appears more psychologic than real when tested in the light of unprejudiced experience."—Souders, Hunscher, Hummel, and Macy; Am. J. Dis. Child. 58:529, Sept., 1939.

STUDIES like that quoted above indicate that the milk needs of older children may be met with entire adequacy when Irradiated Carnation Milk is used both for drinking and in cooked foods. In a 1:1 dilution, a glass of Carnation Milk offers the child all the important food values of whole milk, plus a significant enrichment with vitamin D. Safety, uniformity, ready digestibility and economy are added factors recommending this course. . . . There seems to be no important dietary reason, in the light of present-day knowledge, for changing to any other form of milk when an infant outgrows its Irradiated Carnation Milk formula. . . . *Carnation Company, Milwaukee, Wis.; Toronto, Ont.*

Irradiated
CARNATION MILK
"From Contented Cows"

DURING PREGNANCY AND LACTATION

Supply Extra Calcium

this pleasant, effective way

IT is generally recognized that calcium and phosphorus metabolism, during pregnancy and lactation, is subjected to extra demands. Since the infant depends upon the mother for these essential elements and because many of the foods commonly used in the American diet are low in calcium, it is often desirable to prescribe an effective dietary supplement.

In Dicalcium Phosphate Compound with Viosterol Squibb the physician has at his disposal a product which presents a readily absorbed and suitably balanced source of calcium and phosphorus, with sufficient Vitamin D to assist in their utilization.

Dicalcium Phosphate Compound with Viosterol Squibb is available in both tablet and capsule form. The tablets are flavored with wintergreen and have a very pleasant taste. The capsules are useful as a change from the tablets, especially during pregnancy and lactation which may require routine use of a calcium preparation over an extended period of time.

One tablet (or two capsules) contains 9 grains dicalcium phosphate, 6 grains calcium gluconate and 660 U.S.P. XI units of Vitamin D. The usual dose for pregnant and lactating women is one or two tablets (2 or 4 capsules) t. i. d. Tablets are available in boxes of 51 and 250; capsules in bottles of 100 and 1000.

For literature address the Professional Service Department, E. R. Squibb & Sons, 745 Fifth Avenue, New York, N. Y.

SQUIBB

Dicalcium Phosphate Compound with Viosterol

TABLETS · · · CAPSULES

VITAMIN B COMPLEX
in Winter Infections

YEAST VITAMIN
(HARRIS)
Patents applied for
Prepared from fresh brewers' yeast (Saccharomyces cerevisiae). Water-soluble vitamin-B complex. Concentrated. A natural food tonic. Stimulates appetite.
Prepared by
THE HARRIS LABORATORIES
Tuckahoe, New York

Bottles of 50, 500, 1000.

WINTER COLDS, grippe and pneumonia are mixed infections and can have a basic cause of fatigue, lowered metabolism or deficiency of the vitamins.

Micro-organisms prey upon denuded or depleted tissues and membranes and a deficiency of the water-soluble vitamins can cause this state.

The following data from current medical literature are useful winter observations:

1. Vitamin B_1 stimulates a *natural hunger* and desire for food.

2. In fever—or when the body temperature rises, oxidation and metabolism are accelerated, accompanied by larger requirements of Vitamins B_1 and B_2.

3. Bed-ridden cases are subject to limited or restricted "hospital diet". Dr. Geo. R. Cowgill[1] says that sores or ulcers can appear in patients upon a *restricted diet* and were healed upon feeding Yeast Vitamine (Harris) Concentrate.

Dr. Rose[2] (Yale Med. School) and others have reported cases of infection with Baccillus Welchii, where feeding liberal amounts of Vitamin B Complex built up a "bodily immunity" and the organisms disappeared from the blood stream.

Riddle, Spies and Hudson[3] state that lesions at the corners of the mouth—riboflavin deficiency—infected with Staphylococcus aureus and Streptococcus hemolyticus were healed rapidly upon feeding sources of Vitamin B_2.

Since 1919

YEAST VITAMINE (HARRIS) TABLETS

have been used by physicians. They contain Vitamins B_1-B_2-B_4-B_6 and nicotinic acid. Their therapeutic effects are greater than with the individual vitamins.

Also BREWERS' YEAST AS POWDER OR 7½ GRAIN BLOCKS. TABLETS OF THIAMIN CHLORIDE–RIBOFLAVIN–NICOTINIC ACID–ASCORBIC ACID.

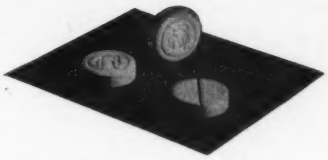
1 Archiv. of Path., Feb. 1929.
2 Soc. Exp. Biol. & Med., May 1929.
3 Soc. Exp. Biol. & Med., 45-361, 1940.

THE HARRIS LABORATORIES
TUCKAHOE NEW YORK
SINCE 1919
FOUNDERS of VITAMINS for MEDICAL USE

A New Development

ORAL TABLETS

OF MALE SEX HORMONE



NEO-HOMBREOL (M) tablets, methyl testosterone 'Roche-Organon,' now make possible effective oral replacement therapy of male sex hormone deficiency. Three to four 10-mg. Neo-Hombreol (M) tablets by mouth are equivalent to 10 mg. testosterone propionate by injection. The marked oral effectiveness of methyl testosterone, amply demonstrated in experimental and clinical studies alike, vastly increases the convenience of male sex hormone medication. In the words of one investigator, oral administration of methyl testosterone "may ultimately replace all other methods of using testosterone or its propionate." (Foss, *Brit. M. J.*, 1939, 2:11).

Neo-Hombreol (M) tablets may be prescribed in all conditions in which male sex hormone therapy is indicated, such as eunuchism (including cases of castration), hypogonadism (eunuchoidism), and male climacteric symptoms (impotence, etc.) in men, and certain cases of hypermenorrhea, dysmenorrhea, intermittent mastopathia, menopausal disturbances, and for the suppression of lactation in women. Physicians are invited to write for a special descriptive leaflet giving dosage recommendations.

• Neo-Hombreol (M) tablets, 10 mg. methyl testosterone each, are individually wrapped in sanitape and packaged in cartons of 15 and 30. (Note: Methyl testosterone is also highly active by cutaneous absorption. For use by inunction, Neo-Hombreol (M) Dosules are available, each containing 2 Gm. absorbable ointment base incorporating 4 mg. methyl testosterone, in boxes of 25).

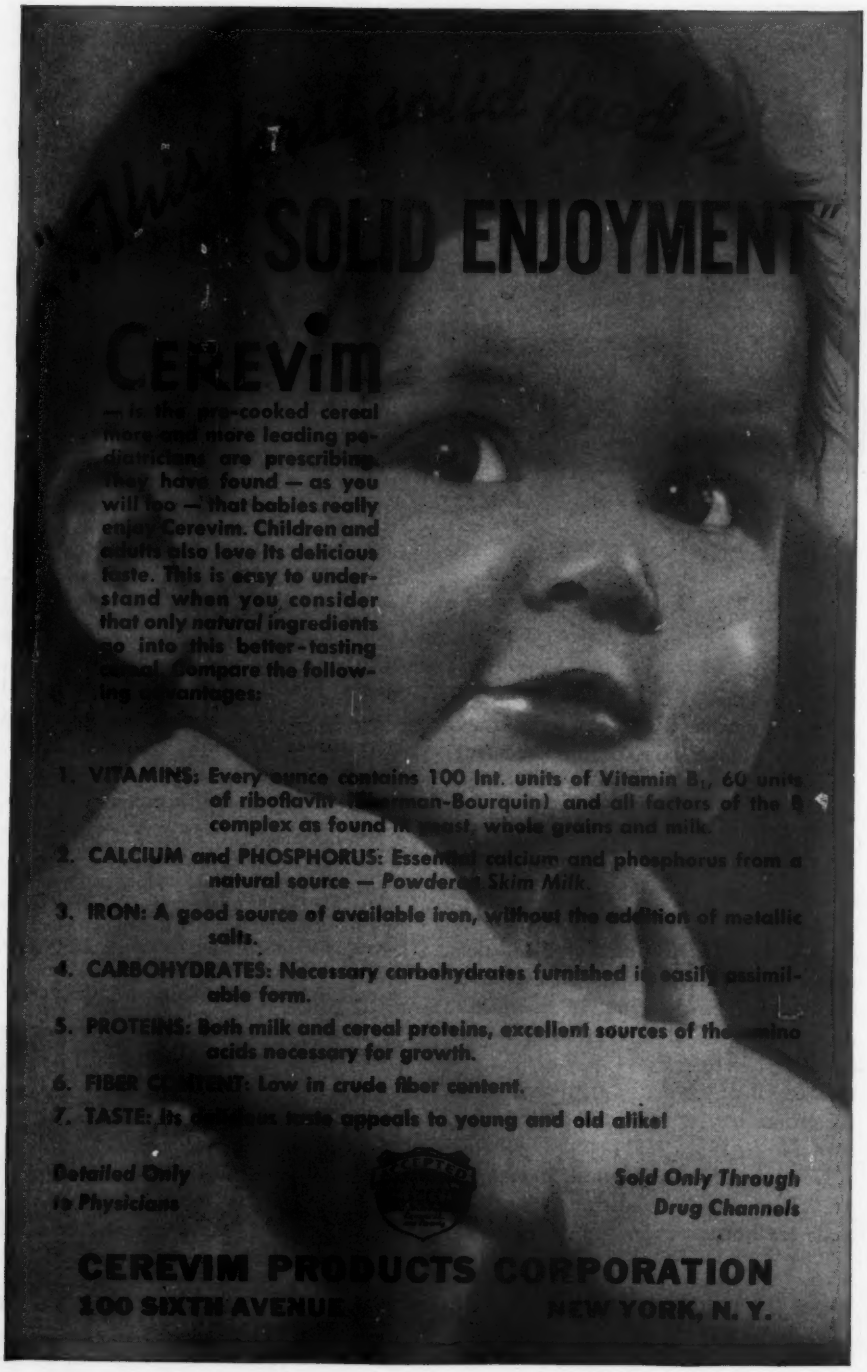
NEO-HOMBREOL (M) TABLETS

(Methyl Testosterone)

EFFECTIVE ORAL THERAPY

ROCHE-ORGANON, INC. • NUTLEY • NEW JERSEY

In Canada: ROCHE-ORGANON, LTD. • MONTREAL • TORONTO


SOLID ENJOYMENT
CEREVIM
— is the pre-cooked cereal
1. VITAMINS: Every ounce contains 100 Int. units of Vitamin B1, 60 units
of riboflavin (Warburg-Christian-Bourquin) and all factors of the B
complex as found in yeast, whole grains and milk.
2. CALCIUM and PHOSPHORUS: Essential calcium and phosphorus from a
natural source — Powdered Skim Milk.
3. IRON: A good source of available iron, without the addition of metallic
salts.
4. CARBOHYDRATES: Necessary carbohydrates furnished in easily assimil-
able form.
5. PROTEINS: Both milk and cereal proteins, excellent sources of the amino
acids necessary for growth.
6. FIBER CONTENT: Low in crude fiber content.
7. TASTE: Its delicious taste appeals to young and old alike!
Detailed Only
to Physicians
Sold Only Through
Drug Channels
CEREVIM PRODUCTS CORPORATION
100 SIXTH AVENUE NEW YORK, N. Y.

A Reminder from Borden about

SOUND INFANT NUTRITION

IN BIOLAC—the *liquid* modified milk for infants—sound nutrition and ease of digestion are assured by four key principles.

1. **Fat Adjustment**—fat is reduced to a moderate, more readily assimilable level than found in cow's milk, and is homogenized to provide smaller, more readily digestible droplets.

2. **Protein Adjustment**—protein is maintained at higher level than in breast milk to compensate for biological difference of cow's milk protein, and to provide amply for the greater needs in early months when growth is fastest.

3. **Carbohydrate Adjustment**—as in breast milk, carbohydrate for the growing young is provided solely by lactose, and in Nature's own equilibrium of 60% beta, 40% alpha lactose.

4. **Vitamin and Iron Adjustment**—vitamins A, B_1, D, and iron are provided at recognized prophylactic levels, making their ingestion automatic and certain.

Needing only simple dilution with boiled water, Biolac assures a sterile formula—even including the carbohydrates. It is sold only in drug stores; no feeding directions are given to the laity.

● Please enclose professional card or letterhead when requesting literature or samples. The Borden Co., 350 Madison Ave., New York City.

Borden's **BIOLAC**

A BORDEN PRESCRIPTION PRODUCT

Petrolagar*

Helps establish habit time

● The establishment of Habit Time for bowel movement may be aided by the use of Petrolagar Plain.

As part of a complete program for treatment of constipation, Petrolagar contributes to the restoration of normal bowel movement by softening fecal mass.

Petrolagar induces comfortable evacuation which tends to encourage the development of a regular "HABIT TIME."

**Petrolagar—The trademark of Petrolagar Laboratories, Inc., brand emulsion of mineral oil . . . Liquid petrolatum 65 cc. emulsified with 0.4 gm. agar in menstruum to make 100 cc.*

Petrolagar Laboratories, Inc. • 8134 McCormick Boulevard • Chicago, Illinois

NICOTINIC ACID AND PELLAGRA

DESPITE the striking reduction in mortality achieved during the past few years, pellagra still remains one of the most serious deficiency diseases in the United States, from the standpoint of number of persons affected and economic losses entailed.

The administration of nicotinic acid or nicotinic acid amide in adequate dosage to patients with acute pellagra results in the prompt disappearance of alimentary, dermal, and other lesions characteristic of the disease. Dramatic and profound improvement occurs in the mental symptoms of pellagra. It is pointed out, however, that nicotinic acid has no effect on the polyneuritis which so often accompanies pellagra. When this is present, it may be necessary to administer thiamine hydrochloride or ensure a diet rich in vitamin B_1.

The optimal dosage of nicotinic acid or nicotinic acid amide probably varies considerably in different cases, depending upon the severity of the deficiency. Experience with large series of cases, however, has demonstrated that the oral administration of 500 milligrams daily, in ten doses of 50 milligrams each, is safe and effective for the average adult with pellagra. Administered parenterally, the total daily dose may vary from 40 to 80 milligrams, dissolved in sterile physiologic solution of sodium chloride and injected intravenously in divided doses of 10 to 15 cc. each.* Oral administration appears to be preferable to parenteral therapy unless absorption from the gastro-intestinal tract is thought to be significantly impaired.

*Spies, T. D., Vilter, R. W., and Ashe, W. F.: J. A. M. A. *113:* 931-937, Sept. 2, 1939.

Literature on request

Also Available, Nicotinic Acid Amide Merck

NICOTINIC ACID MERCK

Council Accepted

RIBOFLAVIN DEFICIENCY IN MAN

"The nonexperimental cases of riboflavin deficiency in man seen by Oden, Oden, and Sebrell and by Spies and his associates have occurred in the South, where pellagra is endemic. The fact that 10 cases were recorded by us in New York City before we recognized the true nature of the lesions, and the fact that since Sebrell and Butler's report we have seen an average of 1 case per month on this service, while the average admissions were 272 per month, indicate, however, that the disease may be not uncommon in the northeastern states."

—Jolliffe, N., Fein, H. D., and Rosenblum, L. A., Riboflavin deficiency in man, N. England J. Med. *221:* 921-926, Dec. 14, 1939.

THE significance of riboflavin in human nutrition has not been fully determined, but recent studies indicate that it is essential for man. Sebrell and Butler[1] have produced lesions in human subjects maintained on an experimental diet deficient in riboflavin. The lesions disappeared following administration of synthetic riboflavin, reappeared following withdrawal of riboflavin, and again disappeared following treatment with riboflavin.

Naturally occurring riboflavin deficiency with lesions similar to those described by Sebrell and Butler has been reported by several investigators[2, 3, 4, 5] and Jolliffe and his associates[6] have recently described 15 cases of riboflavin deficiency which occurred in New York City. Lesions in these patients were similar to those produced experimentally by Sebrell and Butler, but were more advanced. The lesions were unimproved by nicotinic acid, but responded to riboflavin.

1. Sebrell, W. H., and Butler, R. E.: Pub. Health Rep. *54:* 2121-2131, Dec. 1, 1939; *ibid. 53:* 2282-2284, Dec. 30, 1938.
2. Hogan, A. G.: J. A. M. A. *110:* 1188-1193, April 9, 1938.
3. Spies, T. D., Vilter, R. W., and Ashe, W. F.: J. A. M. A. *113:* 931-937, Sept. 2, 1939.
4. Oden, J. W., Oden, L. H., and Sebrell, W. H.: Pub. Health Rep. *54:* 790-792, Dec. 1, 1939.
5. Spies, T. D., Bean, W. B., and Ashe, W. F.: Ann. Int. Med. *12:* 830, May, 1939.
6. Jolliffe, N., Fein, H. D., and Rosenblum, L. A.: N. England J. Med. *221:* 921-926, Dec. 14, 1939.

RIBOFLAVIN MERCK

Council Accepted

MERCK & CO. Inc. *Manufacturing Chemists* RAHWAY, N. J.

"...Casein Modified"

ACCEPTED AMERICAN MEDICAL ASSN. Council on Foods and Nutrition

Made from fresh skim milk (casein modified) with added lactose, salts, milk fat, and vegetable and codliver oils.

In human milk 2/3 of the protein is in true solution, while in cow's milk only 1/6 of the protein is soluble. During the process employed in preparing Similac the soluble proteins in cow's milk are increased to a point approximating the soluble proteins in human milk. How greatly this improves the digestibility is indicated by a comparison of the curd (insoluble calcium paracaseinate) formed by cow's milk, with the soft flocculent curd of Similac. The softer the curd the shorter the digestive period.* Similac, like breast milk, has a consistently zero curd tension.

* Espe & Dye—"Effect of Curd Tension on the Digestibility of milk"—Amer. Journal Diseases of Children—1932, Vol. 43, p. 62.

SIMILAC } SIMILAR TO BREAST MILK

M&R DIETETIC LABORATORIES, INC. • COLUMBUS, OHIO

SULFATHIAZOLE Winthrop

Another IMPORTANT CHAPTER *in* ANTIBACTERIAL CHEMOTHERAPY

SULFATHIAZOLE constitutes an additional triumph of chemotherapeutic research which has proved of great value to clinical medicine.

PNEUMOCOCCUS INFECTIONS . . . Thousands of cases of pneumococcus pneumonia have responded with dramatic promptness to Sulfathiazole. In comparison with its pyridine analogue, Sulfathiazole is less likely to cause serious nausea or to provoke vomiting.

STAPHYLOCOCCUS INFECTIONS . . . With Sulfathiazole, the mortality rate of staphylococcus septicemia has been strikingly reduced. Thus, in a series of fifteen reported cases, all of the patients recovered.

GONOCOCCUS INFECTIONS . . . Early cessation of discharge and a high percentage of cures have been reported. Success has been observed in cases resistant to other chemotherapeutic agents.

Write for literature which discusses the indications, dosage and possible side effects of Sulfathiazole.

Specify **SULFATHIAZOLE WINTHROP**

ACCEPTED AMERICAN MEDICAL ASSN

HOW SUPPLIED: Sulfathiazole-Winthrop is supplied in tablets of 0.5 Gm. (7.72 grains); also (primarily for children) in tablets of 0.25 Gm. (3.86 grains).

For preparing test solutions, powder in bottles of 5 Gm.

Winthrop CHEMICAL COMPANY, INC.

Pharmaceuticals of merit for the physician

NEW YORK, N. Y. - WINDSOR, ONT.

7553E

IN HIGH POTENCY
Whole Vitamin B Complex in Teaspoonful Dosage
No half-way measure, this . . . for clinical experience is showing that vitamin B deficiencies are usually *complex* deficiencies, responding more quickly and completely when *all* factors of the B complex are given.
ELIXIR
BETA-CONCEMIN
MERRELL
Now more potent than before, with no increase in price.
In small dosage of one teaspoonful three times daily, it supplies 1000 International Units vitamin B_1, 2000 gammas vitamin B_2, 15 milligrams nicotinic acid amide, 450 gammas vitamin B_6, with 225 gammas pantothenic acid, factor W and other components of vitamin B derived from liver.
Palatable as well as potent:
The pleasant, fruity flavor of Elixir Beta-Concemin appeals to both children and adults . . . a real aid to patient cooperation. Available at prescription pharmacies in 4 oz. and 12 oz. bottles.
In tablets, too:
Each Beta-Concemin Tablet is equal in vitamin B potency to one-half teaspoonful of the Elixir. Bottles of 100 and 1000.
Write for literature and sample
THE WM. S. MERRELL COMPANY
Founded 1828 • CINCINNATI, U. S. A.

PLASMA & SERUM

prepared with BAXTER EQUIPMENT

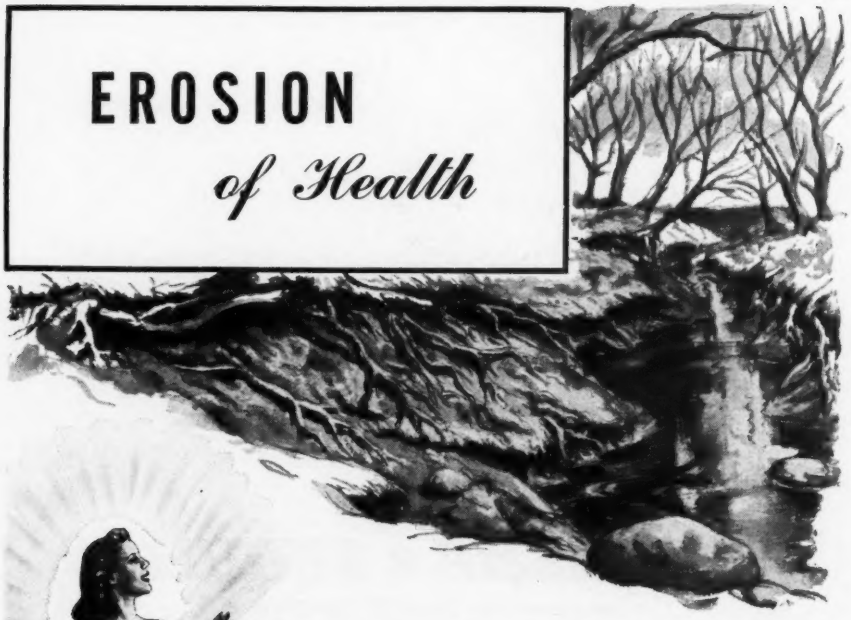
Plasma and serum costs but little when prepared with SIMPLE, SAFE AND COMPLETELY CLOSED *Baxter vacuum equipment. Blood is drawn from donor into a Baxter Centri-Vac for sedimentation or centrifugation. The plasma or serum is then aspirated into a Baxter Plasma-Vac for dispensing, storing, or for transporting—* SEALED IN VACUUM. *Write for Brochure "PSC" containing information on preparation, and abstracts regarding use for burns, shock, hemorrhage, and hypoproteinemia, etc.*

**ALSO SERUM*

THE BAXTER CENTRI-VAC AND PLASMA-VAC

Products of
BAXTER LABORATORIES
Glenview, Ill.; College Point, N.Y., Glendale, Cal.; Toronto, Canada; London, England
Produced and distributed in the
Eleven Western States by DON BAXTER, INC., Glendale, Cal.
Distributed East of the Rockies by
AMERICAN HOSPITAL SUPPLY
CHICAGO CORPORATION NEW YORK

EROSION *of Health*



THE persistence of such relatively minor symptoms as lack of endurance, malaise fever sores, or aphthae, and tendency to skin eruptions may be the evidences of a nutritional deficiency that will in time erode the foundations of health. Some degree of anemia and manifestations of vitamin B complex deficiency are frequently present.

For such cases, LIVER and YEAST CONCENTRATE *Armour* often proves a valuable nutritional adjuvant. It contains the hematopoietic and vitamin principles of both liver and yeast. The characteristic odor and taste of liver have been largely eliminated. The preparation is palatable and free from gastro-intestinal irritants. The anti-anemic properties of liver and the vitamin B complex factors have been fully preserved in the processing.

LIVER and YEAST CONCENTRATE *Armour* may be used to advantage during pregnancy and lactation. In the secondary anemias, chlorosis, etc., some form of iron may be simultaneously administered since clinicians have found that iron medication is more effective when given with liver and yeast.

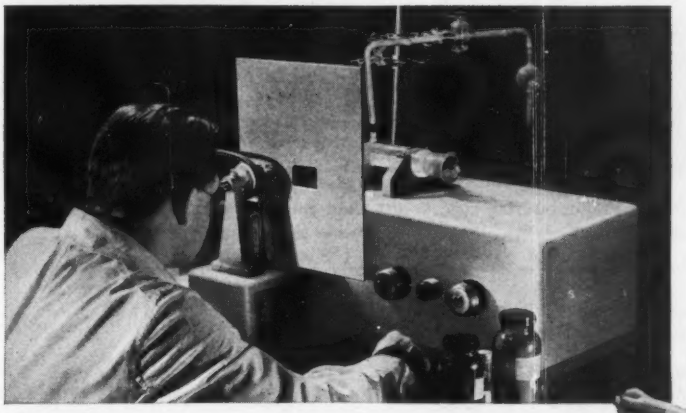
The average adult dose is two teaspoonfuls twice daily, in a little water, milk, or fruit juice.

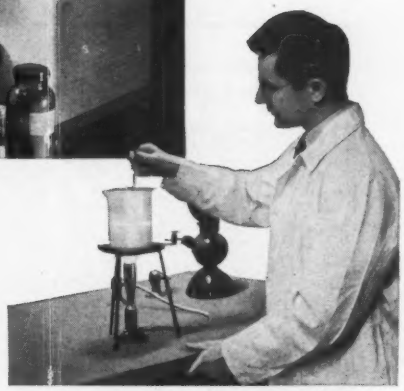
Armour
LIVER and YEAST CONCENTRATE

The ARMOUR LABORATORIES
CHICAGO, ILLINOIS

HOW YOU PROFIT FROM THE

"UNSEEN" IMPROVEMENTS IN PATTERSON X-RAY SCREENS!





X-RAY SCREEN RESEARCH to be successful can never be spasmodic. It must be carried on, day in and day out, year after year. In this way, seemingly small improvements have been *continually* embodied in Patterson Screens without any official announcement. In other words, the performance of a Patterson Screen you buy today, is *better* than the performance of the *same* type of screen when first made available.

This continuous-research policy of Patterson Screen Company keeps a staff of technical men busy on production and inspection as well as on fundamental research. For example, afterglow is now being studied with the aid of the newly developed Phosphoroscope shown above. Special instruments are utilized to determine the purity of base chemicals. Special care must be taken to eliminate every screen that does not match the standard.

As a result, the exceptionally high quality and uniformity of Patterson Screens is unquestioned. There has been a steady improvement in their wear-resisting properties. Other more evident developments have been greater speed, finer detail and a combination of both.

The worth of this Patterson Research policy is self-apparent, for it has brought to the medical profession the highest possible screen quality and resultant improvements in X-Ray diagnosis.

THE PATTERSON SCREEN COMPANY
TOWANDA, PA., U. S. A.

Patterson · WORLD'S STANDARD FOR HIGHEST SCREEN QUALITY

How to Use S-M-A Powder

EACH PACKAGE OF S-M-A* CONTAINS ONE MEASURING CUP

1 Empty one tightly packed measuring cup of S-M-A powder into bottle.

2 Add enough warm previously boiled water to make one ounce.

3 Cap bottle and shake powder into solution. Feed at body temperature.

4 Easy, isn't it?

S-M-A READY TO FEED PROVIDES:

● 20 calories to the ounce, but more important, the nutritional value of S-M-A is that of a complete well-balanced food. When prepared as above, each quart provides:

10 mg. Iron and Ammonium Citrate
200 I. U. of vitamin B_1
400 I. U. of vitamin D
7500 I. U. of vitamin A

NORMAL INFANTS RELISH S-M-A—DIGEST IT EASILY AND THRIVE ON IT

*S-M-A, a trade mark of S-M-A Corporation, for its brand of food especially prepared for infant feeding — derived from tuberculin-tested cow's milk, the fat of which is replaced by animal and vegetable fats, including biologically tested cod liver oil, with the addition of milk sugar and potassium chloride; altogether forming an antirachitic food. When diluted according to directions, it is especially similar to human milk in percentages of protein, fat, carbohydrate and ash, in chemical constants of the fat and physical properties.

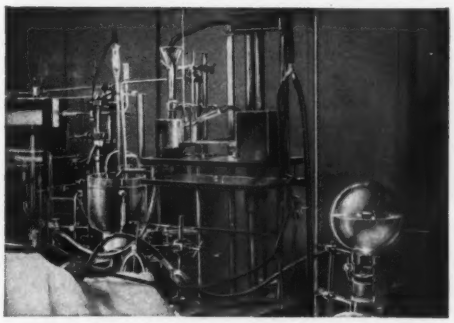
S. M. A. CORPORATION • 8100 McCORMICK BOULEVARD • CHICAGO, ILLINOIS

S3,41.

Scene taken at a Caesarean section with resultant neonatal asphyxia, successfully treated with Coramine.

CORAMINE*
is made EXCLUSIVELY by CIBA

ONLY Ciba manufactures the powerful circulatory and respiratory stimulant, Coramine. Subject of a vast bibliography, here and abroad, Coramine (diethyl amide of nicotinic acid) is the original product which has served so satisfactorily in accident cases, asphyxia, poisoning, "shock," drowning, pneumonia crises, etc. Coramine has seen recent usage in pellagra.



NOTICE—Pictures used herewith are from the film on Coramine. A handsome brochure, "Excerpts From the Film and Additional Clinical Data," will be gladly sent upon request.

*Trade Mark Reg. U. S. Pat. Off. Word "Coramine" identifies the product as the diethyl amide of nicotinic acid of Ciba's manufacture.

Experimental set-up for recording of various factors during experiments with the isolated-heart-lung preparation.

CIBA PHARMACEUTICAL PRODUCTS, INC.
SUMMIT · NEW JERSEY

C · I · B · A

COMPARE...

COCOMALT with other food drinks. *It is not a mechanical mixture.* All ingredients are *malted together* . . . just the vitamins being added under controlled conditions. Precision manufacture plus uniformity is assured through regular biological tests. Clinical work, also, is continuous.

Three servings of COCOMALT per day — made with milk according to directions — give you —

Vitamin A	4200 I. U.
Vitamin B_1	360 I. U.
Vitamin D	402 I. U.
Vitamin G	488 S-B. U.
Calcium	1170 mgs.
Phosphorus	1140 mgs.
Iron	15 mgs.

COCOMALT is used by many leading physicians for undernourished children, pre- and post-operative cases, anorexia of dietary origin, anemias, pregnancy and lactation and numerous other conditions where special dietary needs are indicated.

For normal and therapeutic diets . . . for young and old . . .

COCOMALT is an energizing protective food of vitamin-mineral character. Readily digestible . . . easily assimilated . . . delicious.

R. B. DAVIS COMPANY
HOBOKEN, NEW JERSEY

Cocomalt — THE MALTED FOOD DIETONIC FOR *ALL* AGES

Want short wave diathermy with ALL the benefits?

Choose safe, comfortable INDUCTOTHERMY and get *selective* tissue heating too

When the widely reported effectiveness and usefulness of modern diathermy leads you to thinking of its possible benefits to *your* practice, it will pay you to look well into the extra advantages of Inductothermy. For these are important clinical, convenience, and cost advantages.

Clinically correct Inductothermy heats tissues *selectively* — in proportion to their conductivity. Thereby the greatest amount of heat is generated where it does the most good: primarily in the vascular tissues and muscle, making the treatment of even obese patients safe and comfortable. Tests have shown that Inductothermy heats deeply and adequately, bringing about an active hyperemia so that the optimal results obtainable in the many conditions amenable to heat therapy ensue quickly.

Convenient Extreme simplicity of operation and application are features that eliminate confusion and save valuable time.

Cost The initial cost of Inductothermy is moderate, and its many clinical and economic benefits may even be enjoyed under a convenient budget plan.

For a demonstration of the Inductotherm in your office, or for fuller information by mail, use the convenient coupon today.

GENERAL ELECTRIC X-RAY CORPORATION

2012 JACKSON BLVD. CHICAGO, ILL., U. S. A.

☐ Please arrange with me to demonstrate Inductothermy in my office.

☐ Send me price and details of the Inductotherm by mail.

Name.....

Address.....

City.....

A 24

Smoothage *"An agent which supplies bulk within the bowel (bulk which is smooth, gently stimulating, non-irritating); an agent which re-educates the bowel to normal function and breaks the cycle of catharsis."*

YOU, the physician, know the real value of Smoothage. You know that the mucosal lining of the intestinal tract is a delicate membrane—that stimulation of bowel activity must be gentle, based on the presence of smooth, bland bulk.

You can doubtless affirm, from first-hand experience, the folly of combating constipation with harsh cathartics and irritating roughage materials which so frequently aggravate the existing condition.

Proceeding from these facts, Searle Research has evolved an agent which actually supplies the bulk necessary to overcome sluggishness in the bowel—yet provides it in a form that is gentle, bland and soothing to the irritated mucosa. The product—

METAMUCIL-2

Widely acclaimed in the management of constipation, Metamucil-2 mixes instantly with fluids, and is unusually pleasant to take. May we send you a sample for clinical trial?

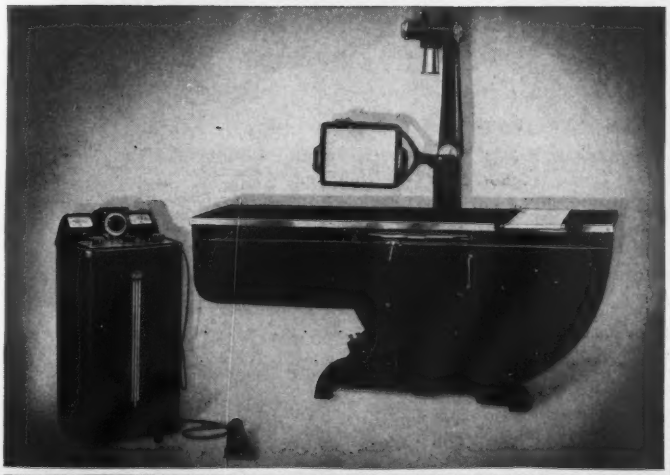
G. D. Searle & Co.

Ethical Pharmaceuticals Since 1888

CHICAGO

New York Kansas City San Francisco

ONE DOCTOR TELLS ANOTHER
JIM, I WISH I HAD YOUR PRACTICE, THEN I COULD PROBABLY AFFORD SOME OF THIS SPLENDID EQUIPMENT, TOO··
WHY, TOM,-IT'S MODERATE PRICE WILL SURPRISE YOU,—ITS DIAGNOSTIC ADVANTAGES WILL INCREASE YOUR PRACTICE AS WELL·
THE WAITE "CENTURY" IS A VERY FLEXIBLE-YET COMPACT UNIT,-TAKES UP LITTLE SPACE··
I UNDERSTAND IT DOES BOTH RADIOGRAPHIC AND FLUOROSCOPIC WORK-IT WOULD BE A GREAT HELP·
ABSOLUTELY!-AND ANOTHER THING; IT IS COMPLETELY SHOCKPROOF AND SIMPLE TO OPERATE · YOU OWE IT TO YOURSELF TO GET A WAITE "CENTURY"



TO ANTICIPATE YOUR REQUIREMENTS FOR YEARS TO COME—A MODERN SHOCKPROOF RADIOGRAPHIC-FLUOROSCOPIC X-RAY APPARATUS HAS BEEN DESIGNED AND BUILT BY WAITE, THE ORIGINATORS OF SHOCKPROOF EQUIPMENT.

PICKER X-RAY CORPORATION
300 FOURTH AVENUE . . . . NEW YORK, NEW YORK
WAITE MANUFACTURING DIVISION CLEVELAND OHIO

MAIL THIS COUPON

PICKER X-RAY CORP.
300 FOURTH AVE., NEW YORK
Gentlemen:
Please send me your new bulletin on the Waite Century.

DR. _____
CITY _____
STATE _____

Wyeth's
REG. U.S. PAT. OFF.

ALULOTION AMMONIATED MERCURY WITH KAOLIN FOR IMPETIGO

Cuts healing time in half
Eliminates greasy ointments

BEFORE TREATMENT: Severe case of impetigo contagiosa, case of J. C., age 8, no prior treatment except washing with soap and water.

AFTER TREATMENT: Wyeth's Alulotion Ammoniated Mercury with Kaolin applied every hour until oozing ceased; then used once a day. (After six days the infection was completely eliminated.)

CONTROLLED CLINICAL TESTS* of which the above is typical, have shown that the healing time in impetigo contagiosa is reduced by half when Wyeth's Alulotion Ammoniated Mercury with Kaolin is used on the impetigo lesions instead of the frequently employed ammoniated mercury ointment.

NO GREASY OINTMENTS are necessary when Alulotion Ammoniated Mercury with Kaolin is used. It contains colloidal kaolin to adsorb and fix the vesicant exudate and thus lessen the tendency of the infection to spread. The ammoniated mercury (5%) exerts a bactericidal effect against the pyogenic organisms involved.

*J. M. Soc. New Jersey, 36, 442 (July) 1939.

Supplied in 3-ounce bottles

JOHN WYETH & BROTHER, INCORPORATED, PHILADELPHIA

"BOUND WATER"

in the

BOWEL

The Cactus—desert plant—despite the aridity of its surroundings, continues to thrive and give succor by storing up a life-sustaining "water balance."

BLAND, non-irritating, non-digestible, the hemicellulose, Mucilose, offers a hydrophilic colloid having the property of *adsorbing and holding water* which causes it to swell like a sponge.

Hence in the bowel Mucilose produces a soft bland mass, which *stimulates peristalsis in a normal physiologic manner by augmentation.*

Note that Mucilose does not interfere with the absorption of vitamins from the intestinal tract, does not impair digestion, does not leak through the anal sphincter. No allergic manifestations have been observed from its use.

Therefore, for the relief of bowel stasis, may we suggest that you prescribe

MUCILOSE

Available for prescription specification as Mucilose Flakes, Mucilose Granules, Mucilose Granules Improved (40% Dextrose).

FREDERICK STEARNS & COMPANY, Detroit, Michigan

NEW YORK • KANSAS CITY • SAN FRANCISCO • WINDSOR, ONT. • SYDNEY, AUSTRALIA

FREDERICK STEARNS & CO.
Detroit, Michigan—Dept. SM-4
Please send me a clinical supply of Mucilose.

Name.....M.D.

Address.....

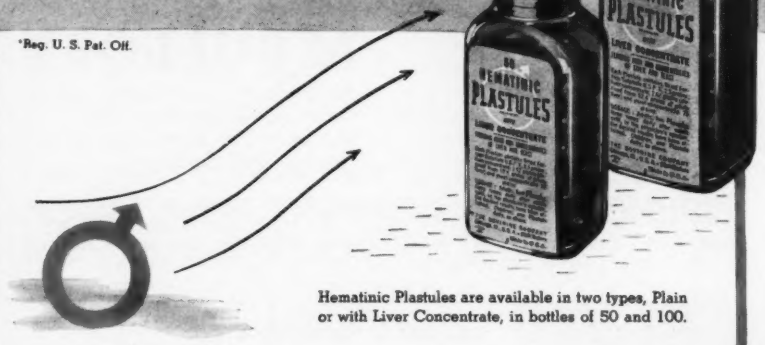
City.....*State*.....

HEMATINIC PLASTULES*

The Modern Iron Therapy

● Hematinic Plastules provide ferrous iron in small soluble elastic capsules—a modern, convenient dosage form. Where iron therapy is indicated, Hematinic Plastules can usually be relied upon to bring about a steady, rapid rise in hemoglobin. Their administration is seldom complicated by gastric disturbance. . . . Hematinic Plastules are an economical iron preparation especially effective for the treatment of the iron deficiency anemia of pregnancy, for chronic blood loss, or post-infection anemia.

*Reg. U. S. Pat. Off.



Hematinic Plastules are available in two types, Plain or with Liver Concentrate, in bottles of 50 and 100.

THE BOVININE COMPANY

8134 McCORMICK BOULEVARD - CHICAGO, ILLINOIS

NICOTINIC ACID (UPJOHN)

The typical dermatitis of pellagra, characterized during its early stages by tenderness and erythema, and subsequently by thickening of the skin, and desquamation, not infrequently involves the lower extremities, especially the anterior aspects of the feet, ankles, legs, and knees.

The administration of nicotinic acid in appropriate doses in cases of pellagra leads not only to the clearing of the cutaneous manifestations of the disease but also to the disappearance of the alimentary lesions and symptoms, and to a profound improvement in the mental symptoms when the latter are the result of inadequate intake of nicotinic acid.

Pellagra, however, is frequently accompanied by evidences of deficiencies of other factors of the vitamin B complex, such as polyneuritis (a manifestation of vitamin B_1 deficiency). In the diets of such patients it may be necessary to insure the presence of foods rich in the vitamin B complex, or to administer—concurrently with the nicotinic acid—thiamine hydrochloride, riboflavin, and, in some instances, pyridoxine hydrochloride.

Nicotinic acid is pyridine-3-carboxylic acid —$C_6H_5O_2N$. It is recognized as a specific in the treatment of the disease of dogs known as blacktongue and in the treatment of human pellagra.

Available at your prescription pharmacy.

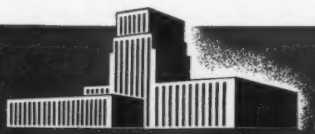
C. T. Nicotinic Acid, 20 mg.

C. T. Nicotinic Acid, 50 mg.

C. T. Nicotinic Acid, 100 mg.

•

In bottles of 100 and 1000



Upjohn

KALAMAZOO MICHIGAN

* *Fine Pharmaceuticals Since 1886* *

SOME 180 TRYING DAYS

Averaging some 180 trying days, the prenatal period offers many possibilities for calcium and other mineral deficiencies, for nausea of pregnancy, for a score of other complications. Daily replenishment of the basic mineral reserve may be successfully accomplished by the administration of Alka-Zane.

Alka-Zane furnishes sodium, potassium, calcium and magnesium in the readily assimilable forms of citrates, carbonates and phosphates. Every heaping teaspoonful of Alka-Zane supplies as much basic calcium as 12 grains of calcium lactate or 18 grains of calcium gluconate. The absence of sulfates in Alka-Zane makes it especially well suited for adjunct treatment with sulfanilamide.

An efficient alkalizer when acidosis complicates the pathologic picture, that is Alka-Zane. A trial supply gladly sent to physicians. Please write on your letterhead.

WILLIAM R. WARNER & CO., INC.

113 WEST 18th STREET • NEW YORK CITY

ALKA-ZANE *for* ACIDOSIS

(Number two in a series of six.)

Common problems in the management of peptic ulcer

"What are you doing to obtain such rapid ulcer healing?"

X-ray examination demonstrates a decrease in the size of the ulcer in 10 days when Amphojel is administered by the continuous intra-gastric drip. Pain is relieved in 8 to 24 hours.

Four striking features of Amphojel, Wyeth's Alumina Gel, are recognized by clinicians:

Amphojel provides prompt relief from pain. It permits rapid healing of the ulcer. It cannot be absorbed and eliminates the hazard of alkalosis. It reduces excess acidity without completely neutralizing the gastric contents.

" " "

Amphojel, Wyeth's Alumina Gel

Fluid Antacid . . . Adsorbent

One or two teaspoonfuls either undiluted or with a little water, to be taken five or six times daily, between meals and on retiring.

Supplied in 12-ounce bottles

AMPHOJEL

Wyeth's

Alumina Gel

For the Convenience of Ambulatory Patients

Wyeth's Hydrated Alumina Tablets

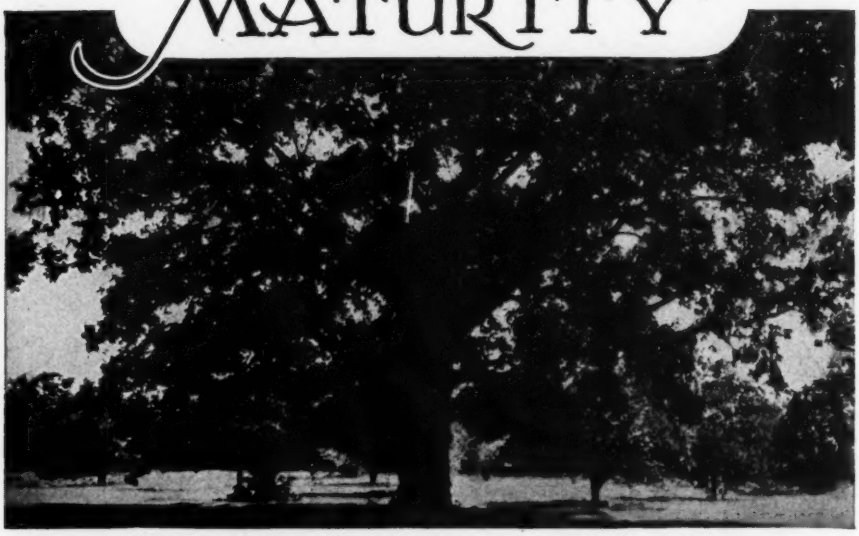
Antacid

One-half or one tablet in half a glass of water. Repeat five or six times daily, between meals and on retiring.

Supplied in boxes of 60 tablets

JOHN WYETH AND BROTHER, INC., PHILADELPHIA, PA.

MATURITY

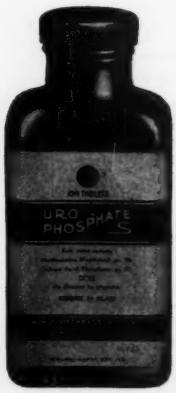


IS SURVIVAL OF THE FIT

URO PHOSPHATE

—for over 21 years a preferred urinary antiseptic

A tablet of methenamine and acid sodium phosphate manufactured and packaged by a process that prevents loss of potency.



Issued in hermetically sealed bottles of 100 tablets

DOSAGE

Two URO-PHOSPHATE Tablets in a glass of water three or four times a day until urine becomes clear. It is desirable to moderately limit fluid intake.

Each tablet of URO-PHOSPHATE contains

Methenamine . . . . . gr. 7½
Acid Sodium Phosphate . . . . . gr. 10

William S. Merrell Co. Inc.
Richmond Virginia

THE TUCKER SANATORIUM, INC.

212 West Franklin St. (Corner of Madison)

RICHMOND, VIRGINIA

This is a private Sanatorium for the Neurological Practice of Drs. Beverley R. Tucker, Howard R. Masters and James Asa Shield.

The Tucker Sanatorium is for the treatment of nervous and endocrine diseases. There are departments of massage, medicinal exercises, hydrotherapy and physiotherapy. The Sanatorium is large and bright, surrounded by a lawn and shady walks, large verandas and has a roof garden. It is situated in the best part of Richmond and is thoroughly and modernly equipped. The nurses are specially trained in the care of nervous cases.

St. Elizabeth's Hospital

Richmond, Virginia

STAFF

J. Shelton Horsley, M.D., Surgery and Gynecology
Guy W. Horsley, M.D., General Surgery and Proctology
Douglas G. Chapman, M.D., Internal Medicine
Wm. H. Higgins, M.D., Consultant in Internal Medicine
Austin I. Dodson, M.D., Urology
Charles M. Nelson, M.D., Urology
Fred M. Hodges, M.D., Roentgenology
L. O. Snead, M.D., Roentgenology
R. A. Berger, M.D., Roentgenology
Helen Lorraine, Medical Illustration

Visiting Staff

Harry J. Warthen, Jr., M.D., Surgery
W. K. Dix, M.D., Internal Medicine
James P. Baker, Jr., M.D., Internal Medicine
Marshall P. Gordon, Jr., M.D., Urology
Howell F. Shannon, D.M.D., Dental Surgery

Administration

N. E. PATE, Business Manager

The operating rooms and all of the front bedrooms are completely air-conditioned.

School of Nursing

The School of Nursing is affiliated with Johns Hopkins Hospital School of Nursing in Baltimore for a three months' course each in Pediatrics and Obstetrics.

Address: Director of Nursing Education

THE TURNER - GOTTEN SANATORIUM

MEMPHIS, TENNESSEE, Route 6, Box 288

For the Diagnosis and Treatment of Mental and Nervous Disorders

Located on the Raleigh-La Grange Road, five miles east of the city limits. Accessible to U.S. 70 (the Bristol Highway). 53½ acres of wooded land and rolling fields. Equipment new and modern, including the latest equipment for physical and hydrotherapy. Special emphasis is laid upon occupational and recreational therapy under the supervision of a trained therapist. An adequate nursing personnel gives individual attention to each patient.

C. C. TURNER, B.S., M.D., Neuropsychiatrist **NICHOLAS GOTTEN, M.D., F.A.C.S., Neurosurgeon**

Grace Lutheran Sanatorium For Tuberculosis

A Beauty Spot on Prospect Hill

701 South Zarzamora Street
SAN ANTONIO, TEXAS

JAMES L. ANDERSON, M.D., Medical Director

Admits patients irrespective of denomination or creed.

Ideal all year climate.—Excellent medical and nursing care.—Radiographic, Fluoroscopic and Pneumothorax service.

New, distinctive, Individual **Bungalows,** highly modern, and **Private Rooms** with baths and sleeping porches, all equipped with radio.—Beautiful grounds.

Moderate rates.

For booklet and information address:

PAUL F. HEIN, D.D.
Pastor and Superintendent

For Patients With Alcoholic Problems

--*The Farm*

A non-institutional arrangement in Howard County, Maryland, for the individual psychological rehabilitation of a limited number of selected voluntary patients with ALCOHOL problems — both male and female — under the psychiatric direction of

Robert V. Seliger, M.D.

CITY OFFICE:

2030 Park Avenue, Baltimore, Md.

Saint Albans Sanatorium

RADFORD, VA.

A modern, ethical institution, fully equipped for the diagnosis, care and treatment of nervous and mental diseases and selected addiction cases. 2,000 feet elevation. Rates reasonable. Occupational and Hydrotherapy Departments.

J. C. KING, M.D. **JAMES KING, M.D.**
FRANK A. STRICKLER, M.D.

ALLEN'S INVALID HOME

Established 1890 **MILLEDGEVILLE, GA.**
For the treatment of

NERVOUS AND MENTAL DISEASES

Grounds 600 Acres — Buildings Brick, Fireproof — Comfortable — Convenient — Site High and Healthful
E. W. ALLEN, M.D., Department for Men
H. D. ALLEN, M.D., Department for Women
Terms Reasonable

Hoye's Sanitarium

"In the Mountains of Meridian"

MERIDIAN, MISS.

Diagnosis and Treatment of Nervous and Mental Diseases, Alcoholic and Drug Addictions. Especially equipped for the Treatment of Mental Disorders. Convalescents, Elderly People and those requiring METRAZOL THERAPY given special monthly rates. Personal supervision of patients. Consulting physicians.

Dr. M. J. L. Hoye, Supt.

Formerly sixteen years Superintendent of East Mississippi State Hospital

Dr. Brawner's Sanitarium

SMYRNA, GEORGIA

(Suburb of Atlanta)

● *For Nervous and Mental Disorders*
Drug and Alcohol Addictions

Approved diagnostic and therapeutic methods. Hydrotherapy, Electrotherapy, Massage, X-Ray and Laboratory.

Special Department for General Invalids and Senile Cases at Monthly Rates.

JAMES N. BRAWNER, M.D., Medical Supt.
ALBERT F. BRAWNER, M.D., Resident Supt.

APPALACHIAN HALL

Asheville, North Carolina

An Institution
FOR
Rest,
Convalescence,
the diagnosis and treatment of
NERVOUS
AND
MENTAL
DISORDERS,
ALCOHOL
AND
Drug Habituation

Appalachian Hall is located in Asheville, North Carolina. Asheville justly claims an unexcelled all year round climate for health and comfort. All natural curative agents are used, such as physiotherapy, occupational therapy, outdoor sports, horseback riding, etc. Five beautiful golf courses are available to patients. Ample facilities for classification of patients. Rooms single or en suite with every comfort and convenience.

For rates and further information write
Appalachian Hall, Asheville, N. C.

WM. RAY GRIFFIN, M.D. M. A. GRIFFIN, M.D.

McGUIRE CLINIC

ST. LUKE'S HOSPITAL

Richmond, Virginia

. . . Medical and Surgical Staff . . .

General Medicine:
James H. Smith, M.D.
Hunter H. McGuire, M.D.
Margaret Nolting, M.D.
John P. Lynch, M.D.

Orthopedic Surgery:
William T. Graham, M.D.
J. T. Tucker, M.D.

General Surgery:
Stuart McGuire, M.D.
W. Lowndes Peple, M.D.
W. P. Barnes, M.D.
Philip W. Oden, M.D.

Pathology and Radiology:
J. H. Scherer, M.D.

Roentgenology:
J. L. Tabb, M.D.
C. D. Smith, M.D.

Obstetrics:
H. Hudnall Ware, Jr., M.D.
H. C. Spalding, M.D.

Urology:
Austin I. Dodson, M.D.
Chas. M. Nelson, M.D.

Eye, Ear, Nose and Throat:
F. H. Lee, M.D.

Dental Surgery:
John Bell Williams, D.D.S.
Guy R. Harrison, D.D.S.

WESTBROOK SANATORIUM

Richmond ***Virginia***

TELEPHONE 5-3245

Department for Men:
J. K. Hall, M.D.

Associates:
O. B. Darden, M.D.
E. H. Alderman, M.D.
E. H. Williams, M.D.
Rex Blankenship, M.D.

Department for Women:
P. V. Anderson, M.D.

The institution is situated just beyond the northern border of the city on United States Highway Number 1.

The scope of the work of the Sanatorium is limited to the diagnosis and the treatment of nervous and mental disorders and to the addictions to drugs and to alcohol. It affords also adequate facilities for rest and upbuilding under medical and nursing supervision.

The medical staff devotes its entire attention to the patients in the Sanatorium.

The institution maintains a school for trained attendants in which instruction in the care of the nervous and mentally sick is emphasized.

There are twelve separate buildings for patients with 130 beds. Such a large group of buildings makes possible the more congenial grouping of patients. Rooms may be had single or en suite, with or without private bath. There are a few small cottages for the use of individual patients.

A comprehensive general physical and nervous examination is made of each patient. A mental examination is made when indicated. The examination is typed and a copy of it is available for the referring physician. Complete dental investigation is a part of the general survey.

A skilled teacher gives practical daily instruction to small groups in the arts and crafts. Helpful and interesting occupation in the out-of-doors is made possible for the men patients in the vegetable and flower gardens, on the truck farm, in the poultry yards, and in the dairy.

There are bowling, tennis, croquet and pool. On Sunday evening there is chapel service.

Detailed information is available for physicians.

STUART CIRCLE HOSPITAL

413-21 Stuart Circle

RICHMOND, VIRGINIA

Medicine:
ALEXANDER G. BROWN, JR., M.D.
OSBORNE O. ASHWORTH, M.D.
MANFRED CALL, III, M.D.
M. MORRIS PINCKNEY, M.D.
ALEXANDER G. BROWN, III, M.D.

Obstetrics:
GREER BAUGHMAN, M.D.
BEN H. GRAY, M.D.
WM. DURWOOD SUGGS, M.D.
SPOTSWOOD ROBINS, M.D.

Ophthalmology, Otolaryngology:
CLIFTON M. MILLER, M.D.
W. L. MASON, M.D.

Pediatrics:
ALGIE S. HURT, M.D.
CHAS. PRESTON MANGUM, M.D.

Surgery:
CHARLES R. ROBINS, M.D.
STUART N. MICHAUX, M.D.
ROBERT C. BRYAN, M.D.
A. STEPHENS GRAHAM, M.D.
CHARLES R. ROBINS, JR., M.D.

Urological Surgery:
FRANK POLE, M.D.
MARSHAL P. GORDON, JR., M.D.

Oral Surgery:
GUY R. HARRISON, D.D.S.

Pathology:
REGENA BECK, M.D.

Roentgenology and Radiology:
FRED M. HODGES, M.D.
L. O. SNEAD, M.D.
R. A. BERGER, M.D.

Physiotherapy
ELSA LANGE, B.S., Technician
MARGARET CORBIN, B.S., Technician

Medical Illustrator
DOROTHY BOOTH

Detailed information furnished physicians.

CHARLOTTE PFEIFFER, R.N. **Superintendent**

CITY VIEW SANITARIUM

For MENTAL and NERVOUS DISEASES and ADDICTIONS

Established in 1907

AN ENTIRELY NEW PLANT ERECTED IN 1922

Separate buildings for men and women, ideally arranged and equipped with every facility for the comfort, care, and treatment of the class of patients received.

It is upon the character of service rendered, rather than upon physical facilities that the reputation of such an institution must rest, and to give every patient the maximum of individual attention and unremitting care at all times is the basic principle of our work. An efficient organization exists in all departments. There is maintained an abundantly sufficient staff of capable nurses, divided into day and night shifts, assuring to every patient constant service through each of the twenty-four hours of the day. At midnight this service is as real as at midday.

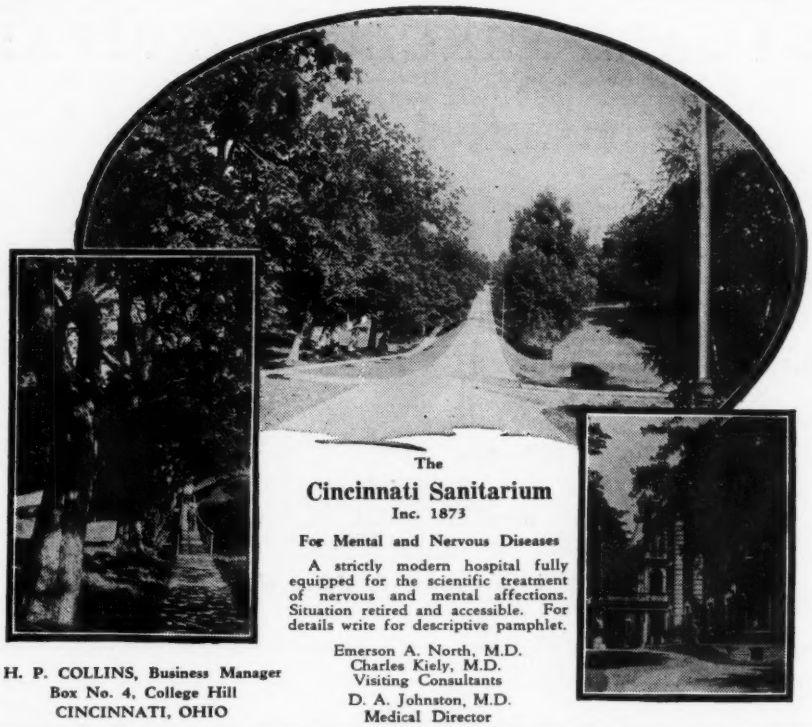
Situated in the midst of a fifty-acre tract and surrounded by a large grove and attractive lawns.

JOHN W. STEVENS, M.D.
Founder

WILL CAMP, M.D
Medical Director

NASHVILLE **R. F. D. No. 1** **TENNESSEE**

Reference: The Medical Profession of Nashville



The

Cincinnati Sanitarium

Inc. 1873

For Mental and Nervous Diseases

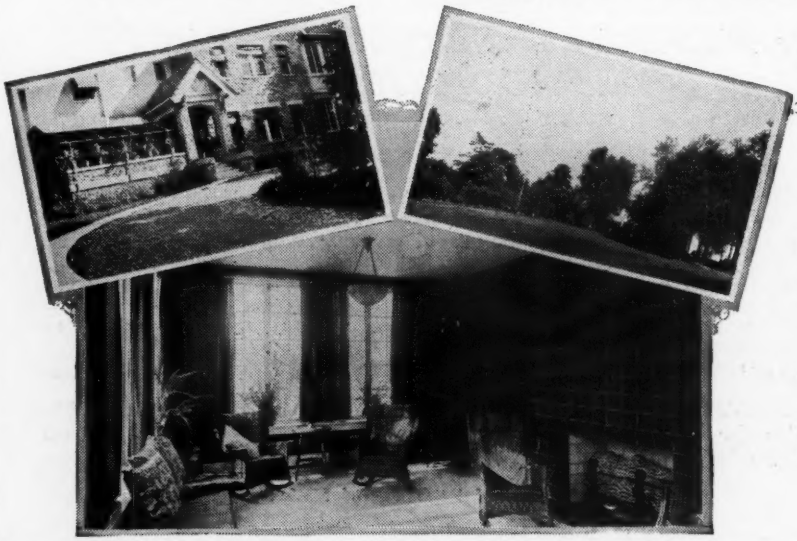
A strictly modern hospital fully equipped for the scientific treatment of nervous and mental affections. Situation retired and accessible. For details write for descriptive pamphlet.

Emerson A. North, M.D.
Charles Kiely, M.D.
Visiting Consultants

D. A. Johnston, M.D.
Medical Director

H. P. COLLINS, Business Manager
Box No. 4, College Hill
CINCINNATI, OHIO

"REST COTTAGE" College Hill, Cincinnati, Ohio



For purely nervous cases, nutritional errors and convalescents.

Completely equipped for hydrotherapy, massages, etc.

Cuisine to meet individual needs.

Emerson A. North, M.D.
Charles Kiely, M.D.
Visiting Consultants

D. A. Johnston, M.D., Medical Director

H. P. Collins, Bus. Mgr., Box No. 4, College Hill, Cincinnati, Ohio

HILL CREST SANITARIUM

FOR NERVOUS AND MENTAL DISEASES AND ADDICTIONS

Metrazol and Insulin Therapy used in Selected Cases. Gradual Reduction Method used in the Treatment of Addictions

Established in 1925

Thoroughly modern in architecture and construction. Eight departments—affording proper classification of patients. All outside rooms attractively furnished. Several bathrooms and rooms with private bath on each floor. Also a spacious sun parlor in each department. Located on the crest of Higdon Hill, 1050 feet above sea level, overlooking the city, and surrounded by an expanse of beautiful woodland. Ample provision made for diversion and helpful occupation. Adequate night and day nursing service maintained.

JAMES A. BECTON, M.D., Physician-in-Charge

P. O. Box 2896, Woodlawn Station, Birmingham, Ala. **Phones 9-1151 and 9-1152**

References: Medical profession of Birmingham and Birmingham Chamber of Commerce.

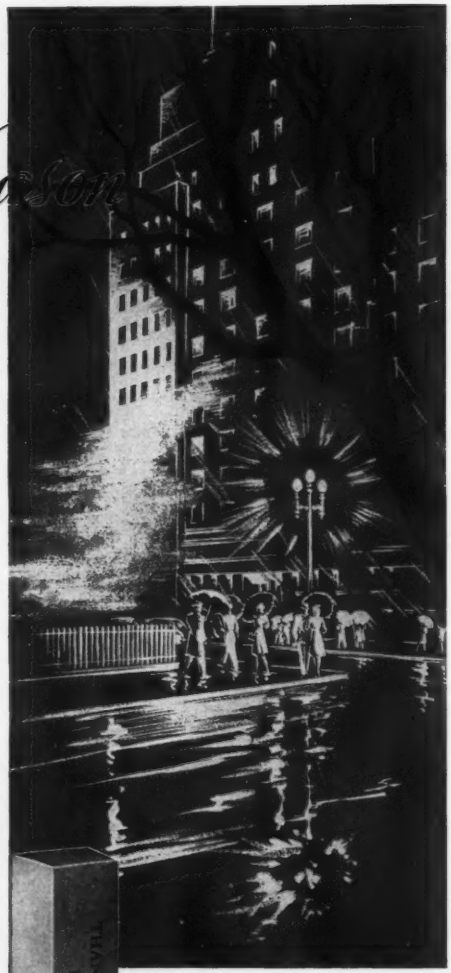
LEONARD D. WRIGHT, M.D.
Medical Director

WALTER R. WALLACE
Business Manager

MEMPHIS **THE WALLACE SANITARIUM** **TENNESSEE**

For over thirty years in successful operation; just eight miles from the heart of the city, in a quiet suburb, occupying sixteen acres of beautiful grounds, this Sanitarium is especially equipped for the treatment of drug addiction, alcoholism, nervous, and mental disorders, the care of patients requiring metrazol and insulin therapy and is ideal for convalescents.

Thantis Season



Wintry weather brings with it the usual prevalence of throat affections.

Thantis Lozenges, H. W. & D., were developed for medical use in the treatment of throat soreness and irritation and following tonsillectomy. They dissolve slowly, permitting prolonged throat medication.

Thantis Lozenges, H.W.&D. are convenient and economical. They are antiseptic and anesthetic for the mucous membranes of the throat and mouth.

Thantis Lozenges contain Merodicein, H. W. & D., 1/8 grain, and Saligenin, H. W. & D., 1 grain.

THANTIS LOZENGES *are supplied in vials of twelve lozenges each.*

HYNSON, WESTCOTT & DUNNING, INC.

BALTIMORE, MARYLAND

SOUTHERN MEDICAL JOURNAL

JOURNAL OF THE SOUTHERN MEDICAL ASSOCIATION

PUBLISHED MONTHLY BY THE SOUTHERN MEDICAL ASSOCIATION AT BIRMINGHAM, ALA.

Volume 34 APRIL 1941 Number 4

BODY SECTION RADIOGRAPHY IN THE DIAGNOSIS OF AORTIC ANEURYSMS AND MEDIASTINAL TUMORS*

By WENDELL G. SCOTT, M.D.
SHERWOOD MOORE, M.D.
and
THOMAS G. RUSSELL, M.D.
St. Louis, Missouri

The purpose of this paper is not to revive a discussion of the methods for the differential diagnosis of thoracic aneurysms and mediastinal tumors, but it is to point out the value of body section radiography as a new method that can frequently be used to help solve this problem. It should be understood that body section radiography is used to supplement the regular diagnostic procedures. It is not intended to supplant any of them. In general, body section films are of value because of one advantage, namely, that the mass and its contiguous structures at any level are pictured in relief. Overlying and obscuring shadows are removed. Thus the observer's attention is automatically focused on the details of anatomy and pathologic changes that are present at the level of the mass.

The principles and technic of body section radiography have been repeatedly described[1] [2] [3] [4] [5] and will be only briefly reviewed. Body section radiography is a term which was introduced by Dr. J. Robert Andrews[6] in 1936 to cover all the different methods of taking x-ray flims through the various sections of a structure. There are several different machines available for this purpose. Among these are the planigraph of Ziedses des Plantes,[7] the stratigraph of Vallebona,[8] the intrascope of the Siemens Company of Germany, and the tomograph of Grossmann and Chaoul.[9] In addition to these, there have been many home-made modifications that are useful for limited purposes, several of which can be adapted to the conventional x-ray tube-stand and Potter-Bucky diaphragm. In this country the x-ray equipment companies now manufacture attachments for their equipment.

The apparatus used in our work was the laminagraph which was invented by Mr. Jean Kieffer,[10] of Norwich, Connecticut, some eleven years ago. In 1936, Dr. Sherwood Moore, working with Mr. Kieffer, constructed the first machine. In order to distinguish this piece of equipment from others that were already available, Dr. Moore coined the word *laminagraph*, derived from *lamina*, meaning *layer*.

It it rather difficult to describe the underlying principle by which we are able to select the layer in a chest that is to be radiographed without showing all the structures lying in front or immediately behind the section selected. During the exposure the x-ray tube and the x-ray film revolve in a circular or spiral path in the same direction, but are out of phase by 90° (*Fig. 1*). The x-ray tube and film are connected by a steel bar. This bar is fastened by means of a swivel joint to the side of the table. During the exposure this steel bar pivots at the swivel joint. The height of the swivel joint above the x-ray table is adjustable in the vertical direction. The height of the swivel joint above the table determines the section that is to be radiographed. By means of this system of linkage, the shadows of the structures in the level of the pivotal point will strike the same spot on the x-ray film irrespective of the position of the x-ray tube and film. At the same time the shadows of the structures above the level of the pivoting point and those below the pivoting point will strike different places on the film during the excursion of the x-ray tube and film and are thus blurred out.

In the roentgen study of patients with intra-

*Read in Section on Radiology, Southern Medical Association, Thirty-Fourth Annual Meeting, Louisville, Kentucky, November 12-15, 1940.

thoracic masses conventional radiographs are made first, usually in the anteroposterior, lateral and oblique positions. From a study of these it is possible to judge the positions and levels at which laminagrams should be made to demonstrate the mass.

The roentgen anatomy of the mediastinal contents can be briefly reviewed by going over the films of this 56-year-old man. The unusual configuration of the heart and the extreme arteriosclerotic changes of the aorta and pulmonary arteries give us an opportunity not only to demonstrate the relationships of these structures in the various positions, but also to compare the information gained from the conventional films with that gained from the sectional films. For future identification note the prominent pulmonary conus and the left pulmonary artery, which can be recognized by the large arteriosclerotic plaques (*Fig. 2 A*). The sectional film (*Fig. 2 B*) brings out the shadows of the pulmonary vascular tree. The vessels lying inferior to the pulmonary arteries are the pulmonary veins. They are of the same density and configuration as the pulmonary arteries and cannot be distinguished from them except by their location. The lateral view (*Fig. 2 C*) shows that the left pulmonary artery runs posteriorly and downward. The same is true of the right pulmonary artery, although it is not distinguishable. In *Fig. 2 D* the added contrast gained by obliterating overlying shadows makes this artery and the pulmonary conus stand out in bold relief. Note how rapidly the artery diminishes in size as it divides into its smaller branches.

The left anterior oblique position (*Fig. 3 A*) pictures the arch, descending aorta, and the left pulmonary artery as it runs across the lower border of the aortic window to the left lung. The laminagram (*Fig. 3 B*) outlines these struc-

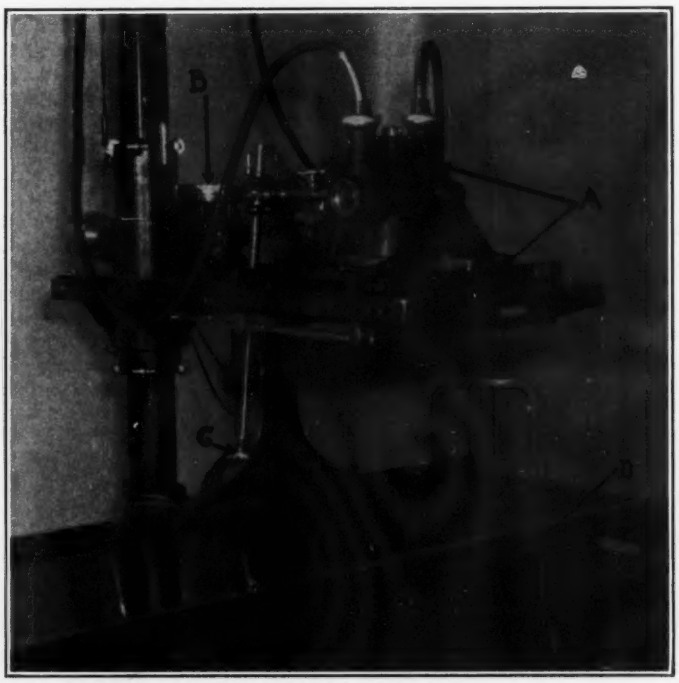


Fig. 1

Photograph of the Kieffer-Moore laminagraph. This is the particular type of body section equipment that was used in this study.

A. X-ray tube mounted on a movable carriage.

B. Motor and turn table for imparting motion to the x-ray tube and film.

C. Swivel joint that is adjustable for vertical shift to select the level at which the body section film is to be made.

D. Movable support for x-ray film.

tures to far better advantage. The trachea, its bifurcation, and the left main bronchus can be easily identified. A second laminagram made at a level several centimeters medial to the previous one will illustrate a cross-section view of the pulmonary artery before it bifurcates.

The right anterior oblique position is used to demonstrate the pulmonary conus, the pulmonary artery in cross-section, and the ascending aorta. At the time this patient was examined, we did not take a right anterior oblique sectional film, and to make a substitution would not be a fair comparison. However, these structures can be well shown, and in addition, the short, right pulmonary artery.

Case 1 is the film of a 60-year-old man with moderate generalized arteriosclerosis of the vascular tree (*Fig. 4 A*). Radiologists are invariably called upon to interpret such bulging shadows in the region of the descending aorta as are pictured in this film. A left anterior oblique film (*Fig. 4 B*) is required to demonstrate that nine times out of ten such shadows are produced by a lengthened and tortuous descending aorta. These arteriosclerotic aortas stand out beautifully on sectional films (*Fig. 4 C*) because their walls are thickened by dense, fibrous tissue and filled with atheromatous deposits. In younger adults the aorta forms a shorter loop; it is smaller in diameter, and it offers little contrast to the

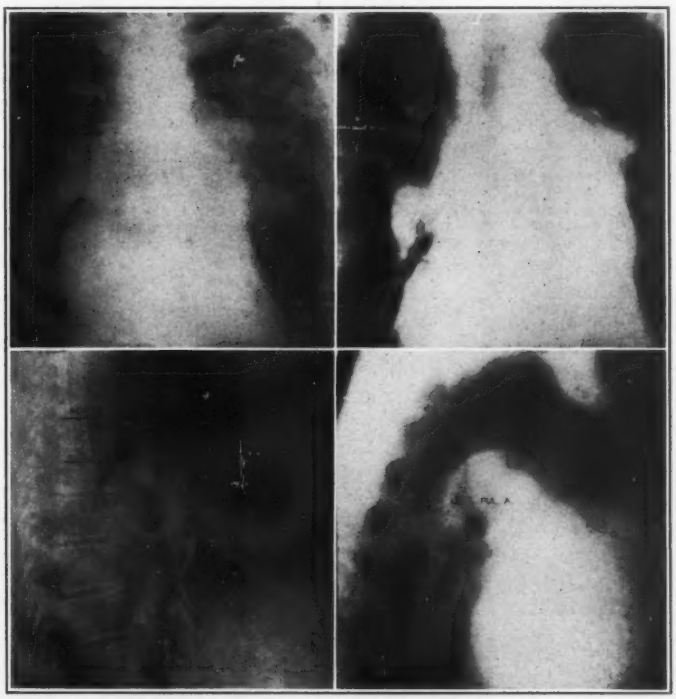


Fig. 2

A, upper left.—Conventional postero-anterior film of chest. On the left the aortic arch, the calcified wall of the pulmonary artery, and the pulmonary conus can all be easily identified. This particular film was selected for this reason so that these structures shown on the conventional and body section films could be more easily identified.

B, upper right.—Postero-anterior laminagram made at the level of the pulmonary vessels. The pulmonary arteries and veins are approximately the same size and density and cannot be distinguished from each other except that usually the pulmonary arteries are more cephalad in location.

C, lower left.—Lateral view of chest. The aortic arch is faintly defined. The left pulmonary artery with the calcification in the walls is easily identified.

D, lower right.—The left lateral laminagram at the level of the left pulmonary artery. The added contrast gained by obliterating overlying shadows brings the left pulmonary artery and the pulmonary conus into bold relief.

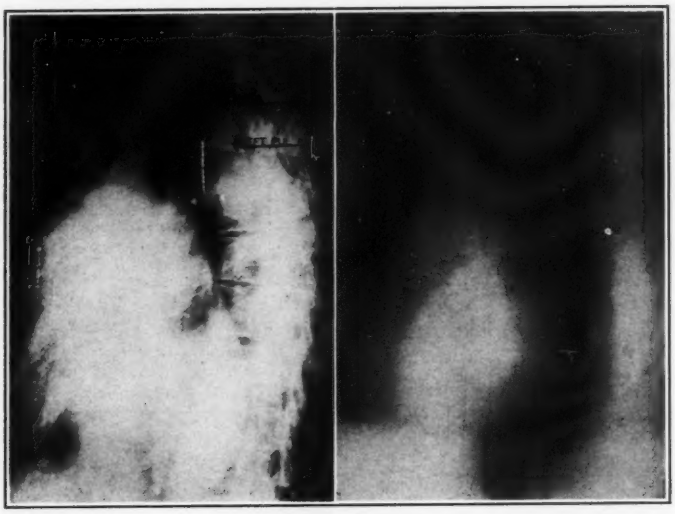


Fig. 3

A, left.—Left anterior oblique film of chest. The aorta can scarcely be visualized, as it offers little contrast to the surrounding structures. The borders of the left pulmonary artery are recognized, but in the absence of the calcification it could not be easily identified.

B, right.—Body section film in left anterior oblique position. The ascending, the arch and the descending portions of the thoracic aorta are clearly visualized in the body section film. The left pulmonary artery is more clearly shown, and the aortic window is thus more accurately delimited. Note the shadow of the trachea and its bifurcation.

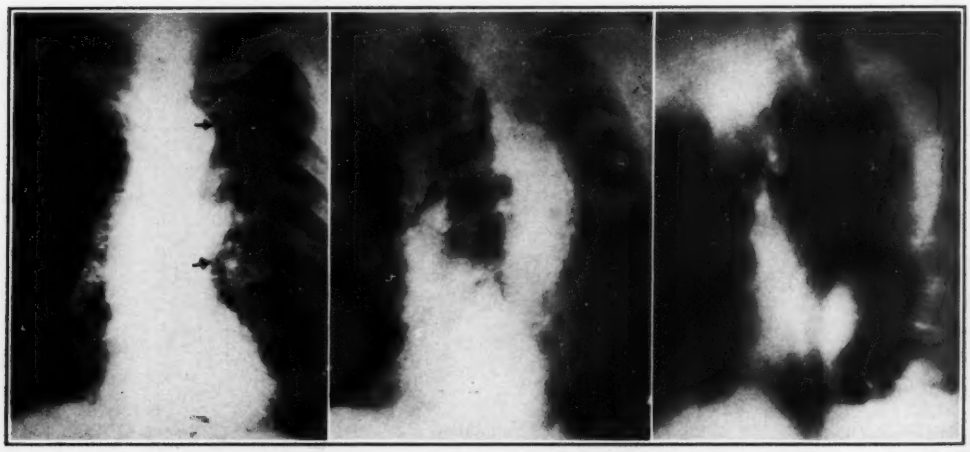


Fig. 4, Case 1

A, left.—Postero-anterior film of chest. The radiologist is frequently called upon to identify a bulging shadow on the left side that extends between the black arrows. This shadow is often confused with aneurysms of the descending aorta.

B, center.—The left anterior oblique film throws into relief the whole arch of the aorta. However, the descending portion of the arch and upper thoracic aorta are poorly defined because of the overlying shadows of the dorsal spine.

C, right.—The body section film in the left anterior oblique projection brings out the detail of the arch and the descending thoracic aorta and also the fact that the shadow is produced by a lengthened and tortuous descending aorta. The more advanced the arteriosclerotic changes, the more beautifully the aorta can be shown on the sectional films. For this reason body section radiography is of more value in the study of elderly patients with cardiovascular disease than in the study of children or young adults.

surrounding tissues. For this reason laminagraphy of the vascular tree has been more useful in the examination of elderly people.

Case 2 is a 69-year-old woman who had a hypertension for many years. Serologic tests were negative. She has had a productive cough for six months and complained of dull pain in the left chest. She has lost twenty-five pounds in the past three months. The conventional film (*Fig. 5 A*) reveals a well defined mass projecting from the mediastinum. The lateral view shows the indistinct outline of a widened and tortuous aorta containing large, arteriosclerotic plaques (*Fig. 5 B*). The body section film (*Fig. 5 C*) brings into sharp relief a large, fusiform, dissecting aneurysm of the descending thoracic aorta. If the aorta were filled with a contrast medium, the aneurysm could hardly be better visualized.

Case 3 is a 74-year-old man with a similar shadow in the region of the descending aorta. He had a luetic aortitis and aortic regurgitation with a positive serum test. He complained of severe, precordial pain. The kymogram recorded large pulsations on the border of the mass. In the oblique view the details of the descending aorta are obscured by the overlying spine. By blurring out the spine on a sectional film it is possible to show the fusiform aneurysm of the descending aorta in better detail. The films of this patient are not illustrated in the paper, as they were very similar to those in *Case 2*.

Case 4 is that of a young man 27 years of age whose chest film revealed a mediastinal mass in the region of the pulmonary conus (*Fig. 6 A*). For about six years he had experienced wheezing spells, shortness of breath on exertion, and a hacking cough. Forceful pulsations were recorded by the kymogram over the left border of the mass (*Fig. 6 B*). Sectional films through the chest brought the mass into sharp focus and thus located it at the level of the pulmonary arteries. The lateral view (*Fig. 6 C*) confirms the location of the mass in the region between the inferior portion of the aortic arch and the pulmonary arteries. It is quite impossible to determine whether the mass is separated from either of these vessels or whether it arises from one of them. The additional contrast and detail afforded by the laminagram through the level of the mass demonstrate that its outlines are continuous with the aorta. This patient was examined when we were beginning the work on body section radiography, and sufficient importance was not placed on this observation. Since we could not be absolutely positive of our diagnosis, and because of the patient's youth, the absence of murmurs and negative luetic tests, the mass was explored on the possibility that it might be a tumor. The surgeon found it to be an aneurysm arising from the ductus arteriosus. Such aneurysms are very rare. Only about a half dozen cases have been reported in the literature. The aneurysm was so intimately connected with both the pulmonary artery and the aorta that it was impossible to remove it. Confidence in any new procedure is gained only through the establishment of such precedents and

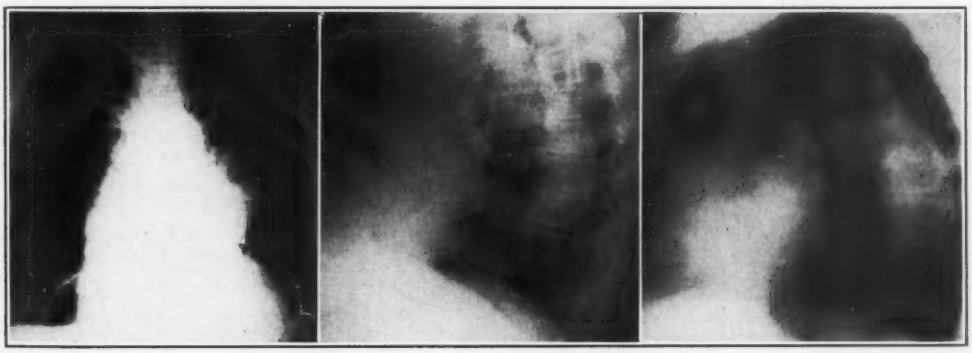


Fig. 5, Case 2

A, left.—Postero-anterior conventional film of a 69-year-old woman. Note a similar bulging shadow in the region of the descending aorta as also noted in Fig. 4 A.

B, center.—The left lateral conventional film shows some dilatation and widening of the descending aorta, but the details are obscured.

C, right.—The body section film in the left lateral position reveals with added clarity the length, size and position of the aorta. Note the large, fusiform aneurysm of the superior portion of the descending thoracic aorta. It is a dissecting aneurysm. The patient's serologic reaction was negative.

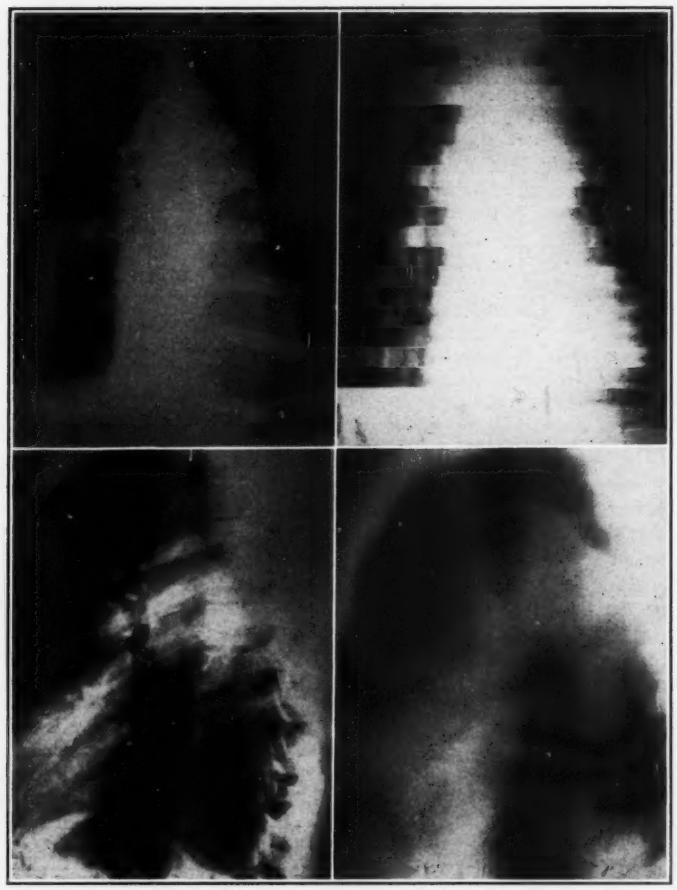


Fig. 6, Case 4

A, upper left.—Postero-anterior film of chest made with Potter-Bucky diaphragm to demonstrate a small rounded shadow overlying the region of the aortic arch and pulmonary conus. This patient is a young man 27 years of age who for six years had experienced wheezing spells, shortness of breath on exertion, and an annoying cough.

B, upper right.—Postero-anterior roentgen kymogram of the heart. Adequate pulsations are recorded by the kymograph over the left border of the heart. It is impossible to say whether these pulsations are expansile or imparted.

C, lower left.—The left lateral film of the chest localizes the mass as occupying the middle third of the mediastinum in the region between the pulmonary artery and the descending aorta.

D, lower right.—Left lateral laminagram made at the level of the mass. The borders of the mass can now be identified as being continuous with the aorta and cannot be separated from it. The aortic window is completely filled by the mass. The pulmonary artery cannot be identified. At operation this mass was found to be a congenital aneurysm arising from the remains of the ductus arteriosus.

antecedents, which in turn build up the sound background of experience. The case we have just described and the one we are about to discuss have been very valuable lessons for us.

In the conventional chest film of *Case 5* is seen a small, rounded shadow projecting from the left of the mediastinum opposite the arch of the aorta (*Fig. 7 A*). Sectional films located the mass at a level just posterior to the pulmonary arteries. The left was displaced slightly downward. On the kymogram pulsations were recorded over the borders of the mass. In the oblique view (*Fig. 7 B*) the mass is very prominent and suggests at once the possibility of a posterior mediastinal tumor. Here again it is impossible to state accurately whether the mass is a tumor or an aneurysm. This patient is a young, vigorous woman, 35 years of age, whose only symptom was a persistent, annoying cough. Luetic tests were negative, and no murmurs were detected. A kymogram was made in the oblique position in an effort to record the pulsations on two sides of the mass simultaneously. From a study of this film it is apparent that both sides of the mass expanded and contracted synchronously. This fact was strong evidence of an expansile lesion, but it was not 100 per cent positive, since an upward displacement of the mass could produce a similar record. The sectional film portrays the mass with superior contrast and detail (*Fig. 7 C*). The mass and the aorta are both in focus and therefore at the same level. Their outlines appear to be continuous. Note the trachea and the left main bronchus. Radiologically the lesion was considered as an aneurysm. From a clinical viewpoint there was no cause for the aneurysm; the patient was young, the physical signs were negative, and the patient's symptoms were of only three months' duration. Because of our limited experience with the laminagraph, we did not feel that we could assume the full responsibility for denying the patient an exploratory mediastinotomy on the possibility that the mass might be a tumor that could be removed. A complicating factor in this decision was a pregnancy which prevented a postponement of the decision if operative procedures were to be carried out. Finally an exploratory operation was agreed upon, and the mass was found to be an aneurysm of the lower portion of the arch of the aorta. Two years prior to the operation this patient had sustained a violent, crushing injury to the chest in an automobile accident. At that time she complained of a severe pain in the region of the mid-dorsal spine. Repeated roentgen examinations of these vertebrae failed to show any definite fracture. After

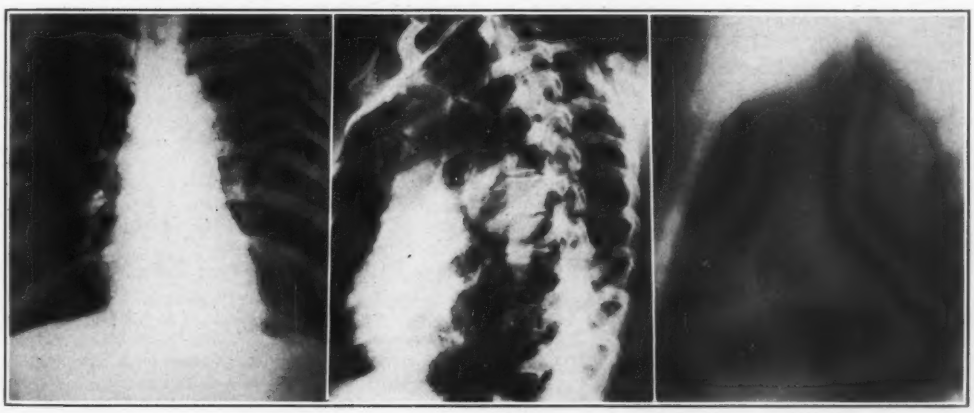


Fig. 7, Case 5

A, left.—Postero-anterior conventional film of the chest. A small mediastinal mass is visualized which is quite similar in location to that shown in Fig. 6. This patient was a young, active woman 35 years of age whose only symptom was a persistent, annoying cough. The serology was negative.

B, center.—In the left anterior oblique position the mass appears to be a posterior mediastinal tumor. It lies back of the trachea and above the left main bronchus.

C, right.—The left anterior oblique laminagram, by obliterating the overlying shadows, brings into greater contrast the shadow of this mass. It is seen to be continuous with the aortic shadow and is apparently a localized fusiform aneurysm as was later proven at operation.

several weeks the pain gradually subsided. While one cannot be sure, the consensus of opinion is that this represents a traumatic aneurysm.

In this presentation we have attempted to point out the value of using body section films in the study of thoracic aneurysms and mediastinal tumors. Body section radiography has the advantage of portraying the level of the mass in relief without overlying and obliterating shadows. In these films the anatomical structures and their relationships at any chosen level can be pictured in far greater clarity.

BIBLIOGRAPHY

1. Moore, Sherwood: Body Section Radiography with the Laminagraph. Amer. Jour. Roentgenol. & Rad. Ther., **39**: 514-522, 1938.
2. Moore, Sherwood: Body Section Radiography with the Laminagraph in Pulmonary Disease. Amer. Rev. Tuberc., **38**: 538-556, 1938.
3. Moore, Sherwood: Body Section Radiography in Surgical Conditions. Amer. Jour. Surg., **46**:309-316, 1939.
4. Moore, Sherwood: Body Section Radiography. Radiology, **33**:605-613, 1939.
5. Kieffer, J.: Analysis of Laminagraphic Motions and Their Values. Radiology, **33**:560-585, 1939.
6. Andrews, R. J.: Planigraphy I: Introduction and History. Amer. Jour. Roent. & Rad. Ther., **36**:575-587, 1936.
7. Ziedses des Plantes, B. G.: A New Method of Differentiation in Roentgenography (Planigraphy). Acta Radiol., **13**: 182-191, 1932.
8. Vallebona, A.: Modified Technique of Roentgenographic Dissociation of Shadows Applied to the Study of the Skull. Radiol. Med., **17**:1090-1097, 1930.
9. Grossmann, G.: Tomography I and II. Fortschr. a. d. Ged. d. Rontgenstrahlen, **51**:61-80 and 191-209, 1935.
10. Kieffer, J.: The Laminagraph and Its Variations: Applications and Implications of the Planigraphic Principles. Amer. Jour. Roent. & Rad. Ther., **39**:497-513, 1938.

DISCUSSION (*Abstract*)

Dr. E. L. Shiflett, Louisville, Ky.—Dr. Scott has been rather modest in his claims for laminagraphy. I personally think it is one of the greatest advancements in x-ray diagnosis in recent years. I want to emphasize the fact that laminagraphy is as applicable to other parts of the body as it is to the diagnosis of aneurysms. We are always surprised at the additional information we obtain when making the examination.

Since the authors have done much to develop this phase of diagnosis, I am sure they will approve emphasis upon the method as much as a discussion of the diagnosis of aneurysms.

In posterior sinus disease it may be very valuable. The posterior sinuses may be demonstrated much better than by the conventional roentgenograms, and may reveal posterior ethmoiditis or sphenoiditis. Routine examination of the posterior sinuses in this manner is far superior to the conventional roentgenographic examination. We now make the conventional as well as the laminagraphic examination of our sinus cases without increasing the cost to the patient. Dr. Moore has stressed the value of laminagraphic examination in sinus disease.

In a left carotid aneurysm, for example, in a tissue layer of two centimeters thickness in the center of a skull measuring 15 centimeters thick in lateral plane, normal structures may be shown on one side and extensive destruction on the other. Slight changes such as a mild degree of hypertrophy of the anterior clinoid and a little parasellar calcification can be shown to better advantage by the laminagraph.

In an elderly individual with pain and a small mass in the region of the right sternoclavicular joint, the conventional roentgenogram showed displacement of the trachea and fibrosis in the apex of the lung mesially which obscured the sternoclavicular articulation. Sections demonstrated very clearly a destructive lesion of the sternal end of the clavicle. The roentgen diagnosis was tuberculosis of the clavicle.

I have merely tried to emphasize the practicability and the applicability to other regions of the body of the method which Dr. Scott has efficiently applied to the study of aneurysms. I believe that in the near future the laminagraph or some modification of it will be considered essential equipment of radiologic laboratories.

Dr. Thomas H. Lipscomb, Jacksonville, Fla.—My interest in body section x-ray was aroused by Dr. Sherwood Moore's excellent movie covering his experimental equipment at the Congress of Radiology held in Chicago a few years ago. The commercially made equipment arising from Dr. Moore's experimental machine is known as the Keleket-Kieffer laminagraph. This sells without tube or energizing equipment for about $4,500.

The purpose of this discussion is to bring before you the fact that satisfactory body section work may be done with relatively inexpensive equipment which can be fabricated by any good local machinist.

The essential principle underlying all body section apparatus involves the simultaneous and correlated movement of x-ray tube and x-ray film in opposite directions during the time of exposure with tube and film pivoting about a fulcrum in the desired plane. In the laminagraph, as used by the essayists in their excellent demonstration, it is possible to use rectilinear motion, circular motion, helical motion or any combination of these motions. The simplified apparatus which I am going to describe is limited to the first named, that is to say, rectilinear motion.

The fulcrum is the most important part of this accessory and consists of a steel box 14 inches long and one inch by one and one-half inches inside dimensions on cross section. The fulcrum is turned on a lathe from a block of steel an inch and one-half square, and rides up and down smoothly inside the steel box. The fulcrum may be moved to any desired position above the table top by means of a screw running the complete length of the box. The steel box is attached at right angles to the ordinary tilting table (in my particular instance a Keleket table) by means of thumb screws which are engaged in the regular slot at the side of the table.

A metal bearing is attached to the Bucky diaphragm at a point corresponding with the level of the film and is fitted with a sleeve through which the linking rod may run.

The rod link consists of a one-inch brass tube which is attached to the tube stand directly below the pivot of the tube stand. Then it passes downward through the bearing on the fulcrum and into the bearing on the Bucky.

My particular tube stand has a friction bearing for rotation of the tube which turns with some difficulty. For this reason, I attached an out-rigger to the tube stand with a piece of airplane cable running downward to the outer end of the tube stand. With this arrangement the weight of the tube carriage is borne equally at each end and the tube rotates freely.

The fulcrum is attached to the side of the table; the link is inserted to the tube carriage, through the bearing in the fulcrum and through the bearing in the Bucky diaphragm; the fulcrum is placed at the approximate level of the desired plane and an exposure of approximately 1.5 time the normal is given. During the time of exposure the tube carriage is moved through an arc of approximately 30°. I have also recently installed an old Engeln Bucky mechanism for moving the tube stand. Several exposures at, above and below the estimated level are usually made.

The total cost of this equipment has not exceeded $75.00. I have photographs of this equipment and will be glad to supply them to anyone who is interested.

As noted previously, this type of apparatus is confined to rectilinear motion and therefore there are certain instances where a special technic is needed which would not be necessary with the more expensive type. A special instance is the sternum where lateral displacement of the patient and film will enable one to avoid the overlying spine and yet have both sides of the sternum on the same plane. This principle should be employed whenever necessary to displace an undesired overlapping shadow from the path of the desired object.

I should like to close with a note of encouragement to those who have not used the body section method. Attack the problem with simple apparatus if you do not feel inclined to invest in a more complicated and expensive one, with the assurance that the results will repay your efforts.

Dr. Scott (*closing*).—I want to thank Dr. Shiflett for bringing out the point that body section radiography, which is the term employed for this procedure irrespective of the apparatus, is used for skeletal studies probably more than it is for chest in our experience. We have found it exceedingly valuable for films of the mandible, for films of the temporomandibular joint, and for lateral views of the dorsal spine.

Dr. Lipscomb has made an ingenious apparatus that will accomplish the same purpose. There are several variations of these home-made devices that are in use over the country, and they serve their purposes very well if they have been accurately put together. He is to be commended on making his machine so that it can be used with the patient standing in the vertical position as well as in the horizontal position.

HIATUS HERNIA OF THE STOMACH*

INCIDENCE, SYMPTOMS AND MEDICAL MANAGEMENT IN 1,220 GASTRO-INTESTINAL CASES

By MOISE D. LEVY, M.D.

and

L. B. DUGGAN, M.D.

Houston, Texas

During the past few years journals of roentgenology and gastroenterology have been replete with reports of cases of diaphragmatic hernia of the esophageal type. The number of articles and the numerous cases reported stand out in marked contrast to the comparative rarity of this condition in the literature prior to 1925. At the Mayo Clinic[1] only thirty cases were reported up to 1925, Carman,[2] in 1924, reporting the ratio in the Mayo Clinic as one to eighteen thousand examinations; yet Harrington,[1] from the same clinic, reported one hundred sixty-one cases of diaphragmatic hernia operated upon between 1926 and 1938, and of these one hundred twenty-three were of the esophageal type. Increased use of the x-ray in routine examinations and improvement in roentgenologic technic undoubtedly account for the rather common finding of this condition at the present time. Knothe,[3] using a special technic at the Charite Hospital in Berlin, reports three hundred cases, representing 8 per cent of all patients subjected to routine gastro-intestinal x-ray examination. The condition has been found so often in elderly patients that Akerlund[4] suggests that the presence of "small, symptomless, sac-less diaphragmatic hernia may be regarded as a normal development accompanying old age."

While there is little doubt that esophageal hernia occurs frequently, the percentage of cases observed in gastro-intestinal x-ray work varies considerably. Ritvo[5] reports sixty cases of hiatus hernia in eight thousand gastro-intestinal cases, a percentage of about 0.8. From the Cleveland Clinic, Root, Pritchett and Clark[6] reported twenty-nine cases in two thousand two hundred and thirteen stomachs examined, a percentage of 1.3. Eisen,[7] in Toronto, reports thirty-three cases in one thousand one hundred and thirty-three routine x-ray examinations of the gastro-intestinal tract, made from January, 1935, to August, 1938. The incidence here was 2.9 per cent. Kantor,[8] in his recent "Synopsis

*Read in Section on Medicine, Southern Medical Association, Thirty-Fourth Annual Meeting, Louisville, Kentucky, November 12-15, 1940.

of Digestive Diseases," says that perhaps three cases of esophageal hernia will be found in every one hundred stomachs examined with the x-ray. We have found twenty-six hernias in one thousand two hundred and twenty cases examined, a percentage of about 2.1.

The hernia which we are discussing may be divided into three anatomical types, according to Akerlund:[4]

(1) The short esophagus type, where we find the esophagus shortened and its lower end as well as the upper part of the stomach permanently in the thoracic cavity. These conditions are congenital and are the result of an embryologic fault. It is interesting to note that recently Shiro and Benjamin[9] reported esophageal hernia in three sisters, and in *Case 2* of the series reported by Bock, Dulin and Brooke[10] the brother was known also to have an esophageal hernia.

(2) In the para-esophageal type, the lower end of the esophagus is in the normal position below the diaphragm, but the fundus of the stomach is herniated through the esophageal hiatus, either behind on either side or surrounding the esophagus. These types are probably all acquired.

(3) The gastro-esophageal type is the commonest type observed. Here we find the upper portion of the stomach as well as the lower end of the esophagus herniated through the esophageal hiatus. This type of hernia is always acquired.

The esophageal foramen is the only one of the three openings in the diaphragm that is completely surrounded by muscle tissue and is thus amenable to dilatation, which explains the occurrence of hernia only through this opening.

Dilatation of the esophageal hiatus has been ascribed to several factors:[4]

(1) Stretching of the hiatus due to an insufficiency of the muscle fibers.

(2) A reduction in the amount of tissue about the hiatus ring.

(3) A decrease in the elasticity of the elastic fibrous tissue about the ring.

(4) Loosening of the connective tissue between the esophagus and peritoneum by intermittent or chronic changes in the intra-abdominal pressure as occurs with coughing, meteorism, constipation with straining at stool, abdominal tumor, and repeated pregnancies. These conditions, either singly or combined, result in a stretching of the muscular and ligamentous tissues about the esophageal hiatus, and are the principal etiologic factors producing hernia through this part of the diaphragm.

Symptoms of hiatus hernia are usually conspicuous by their absence. Diagnosis is made certain in all cases by x-ray study, but a careful history, especially if one is "hiatus conscious," may elicit statements pointing to the presence of this condition. Symptoms vary exceedingly, depending upon the size and type of the lesion, and in the very small hernias there are no symptoms at all. In the thirty-one cases reported by Root[6] *et al.*, referred to above, nineteen cases presented no symptoms, and in our series of twenty-six cases herniation was unsuspected in eighteen.

When present, symptoms may be abdominal, thoracic or constitutional. A common symptom is a feeling of vague distress and discomfort in the epigastrium or just beneath the lower end of the sternum, occurring after a large meal. Pains may simulate typical cholecystic disease or peptic ulcer. The recumbent position increases the severity of the symptoms, and they are usually relieved by belching or effortless vomiting. When brought on by a recumbent position, the symptoms are usually terminated by assuming the upright position.

Thoracic symptoms may consist of a feeling of fullness in the chest after eating, some palpitation of the heart on effort, and occasionally dyspnea and even cyanosis. Typical anginoid pains may be complained of with pain radiating across the chest and down the arms, or into the left shoulder. Ernstene and McGurl[11] recently reported a case of a large esophageal hernia associated with hypochromic anemia and severe anginoid symptoms. Cure of the anemia relieved entirely all the anginoid pains. *Case 1* of our series presented symptoms pointing to cardiac disease. Occasionally, cardiac pains are complained of at night, after lying on the back. Von Bergman[7] refers to this as the "epiphrenal syndrome" and believes that it is due to irritation of the nerve endings in the esophageal hiatus, with reflex manifestations of precordial pain through the sympathetic nervous system. One should always remember, however, that true angina may occur in association with esophageal hernia, one such case having been reported by Root[6] and his associates.

Secondary anemia of the hypochromic type is usually the constitutional effect produced. Bleeding may manifest itself as a frank hematemesis or melena, or it may be insidious and found only by chemical analyses of the stool.

Many articles[9] [10] [11] [12] have appeared associating anemia with esophageal hernia. Bock, Dulin and Brooke,[10] in a most interesting report, cite ten cases of esophageal hernia associated with marked anemia. Three of their cases were operated upon, and in two others autopsies were held. No pathologic condition was found to account for the bleeding, other than the hernia through the diaphragm. They say:

"All patients with esophageal hernia should be considered as potential candidates for anemia, and if anemia is not found at the initial examination, blood studies should be made at intervals to determine if bleeding occurs."

As previously stated, we have observed twenty-six cases of esophageal hiatus hernia, which have been found in studies of one thousand two hundred and twenty gastro-intestinal x-rays. *Chart 1* shows the age, sex, habitus, presenting symptoms and the method used to determine the presence of a hiatus hernia during the x-ray study of our twenty-six cases. The age group is essentially the same as other reports, the youngest being 31 and the oldest 79 years. Twenty of our cases were over 50 years of age and twelve of these were 65 years and over. There were nine males and seventeen females in our group, and, as has been stressed in other reports, most of our cases were either of the full sthenic or hypersthenic habitus.

Only one case was found with an anemia, *Case 14*, which presented symptoms of a bleeding duodenal ulcer, but on x-ray examination the only finding was an esophageal hernia, the duodenum appearing normal under the fluoroscope. Stool examinations were made as a routine on all cases studied, and no evidence of bleeding from the intestinal tract was found in any except

Chart 1

Case No.*	Age	Sex	Habitus	Symptoms Suggest Disease of
1	67	Male	Hypersthenic	Cardiovascular
2	65	Male	Hypersthenic	Cardiovascular
3	57	Female	Full sthenic	Gastro-intestinal, ulcer syndrome
4	27	Female	Full sthenic	Gastro-intestinal, duodenal migraine and irritable colon
5	31	Female	Hyposthenic	Gastro-intestinal, functional, cardiospasm
6	67	Female	Hyposthenic	Gastro-intestinal
7	56	Male	Hypersthenic	Gastro-intestinal, functional spastic colon
8	79	Male	Hypersthenic	Gastro-intestinal, achlorhydria
9	63	Female	Full sthenic	Gastro-intestinal, clinical diagnosis hiatus hernia
10	65	Female	Hyposthenic	Gastro-intestinal, clinical diagnosis hiatus hernia
11	74	Female	Full sthenic	Gastro-intestinal, constipation
12	49	Female	Full sthenic	Gastro-intestinal, clinical diagnosis esophageal hiatus hernia
13	61	Female	Hypersthenic	Gastro-intestinal, ulcer syndrome due to gastritis
14	51	Male	Hypersthenic	Gastro-intestinal, hemorrhage from acute duodenal ulceration
15	65	Female	Full sthenic	Gastro-intestinal, spastic constipation
16	49	Female	Full sthenic	Gastro-intestinal, gallbladder disease
17	68	Female	Hyposthenic	Gastro-intestinal, clinical diagnosis hiatus hernia and spastic constipation
18	67	Female	Full sthenic	Gastro-intestinal, esophageal hiatus hernia
19	62	Female	Full sthenic	Gastro-intestinal, peptic ulcer
20	74	Female	Full sthenic	Cardiovascular, angina pectoris
21	67	Male	Hypersthenic	Gastro-intestinal, diverticulitis of colon
22	63	Female	Full sthenic	Gastro-intestinal, diagnosis indeterminate
23	37	Male	Hyposthenic	Gastro-intestinal, esophageal hiatus hernia plus gastritis
24	41	Male	Full sthenic	Gastro-intestinal, esophageal hiatus hernia
25	64	Female	Full sthenic	Gastro-intestinal, esophageal hiatus hernia
26	65	Male	Hyposthenic	Gastro-intestinal, duodenal ulcer

*The method used in all cases was prone position, right anterior oblique, deep inspiration and expiration.

Case 14. Four of our cases had been x-rayed previously by good roentgenologists, with negative findings relative to esophageal hernia. We have observed, not infrequently, the presence of a hernia fluoroscopically and also demonstrated it upon a film, only to find it impossible to locate any hernia at another examination. This experience has been noted by others and no doubt accounts for the fact that some of our cases had not been diagnosed during previous roentgen studies.

We have found that examination of the patient in the prone position through the right anterior oblique angle is the most satisfactory position for bringing out the presence of an esophageal hernia. Deep inspiration and expiration during the examination will assist in spotting the hernia as the diaphragm moves up and down. Those conditions which should be kept in mind to differentiate from an esophageal hernia are:[7]

(1) Ampullary dilatation of the lower end of the esophagus
(2) Cardiospasm
(3) Ulcer of the esophagus and peptic esophagitis
(4) Cardio-esophageal relaxation
(5) Cancer of the lower end of the esophagus
(6) Diverticulum of the lower end of the esophagus
(7) A diverticulum of the stomach
(8) Hour-glass stomach

We wish to report briefly a few of our cases illustrative of different symptoms accompanying hiatus hernia, with slides made from the films.

Case 2.—W. P., a white man, 65 years old, of the hypersthenic habitus, for about two years had complained of low substernal pain, suggesting cardiac disease. Careful examinations, including repeated electrocardiograms, were negative. Six weeks before our examination he complained of heartburn occurring throughout the day without special reference to meals. Irregular constipation was also present. An Ewald meal removed at the end of forty-five minutes revealed total acid 88, free hydrochloric 58, combined acid 6, acid salts 24, lactic acid and occult blood negative. Blood examination was normal. Hemoglobin was 107 per cent (Sahli) and red blood cells were 5,880,000. The blood Wassermann was negative. Roentgen examination of the gastro-intestinal tract revealed a small esophageal hiatus hernia the size of an English walnut, a spastic colon, and a pathologic gallbladder, with no stones. *Fig. 1* shows the hiatus hernia found. Treatment directed towards relieving the spastic constipation resulted in relief of all symptoms. A cholecystogram made some weeks later revealed a normal concentrating and emptying gallbladder.

Case 9.—Mrs. W. K., a white woman, 63 years old, of the full sthenic habitus, for five years had complained of a sensation of fullness in the epigastrium after meals, intensified by lying down. She had observed that sitting up produced some relief of her symptoms. No gastric analysis was made. Blood count was normal, hemoglobin 84 per cent (Sahli), and red blood count 4,440,000. An x-ray of the gastro-intestinal tract made with the clinical impression of hiatus hernia revealed this to be present, as well as a spastic colon. *Fig. 2* shows the hernia as seen when the patient was in the prone

Fig. 1, Case 2
W. P.—Prone position.

Fig. 2, Case 9
Mrs. W. K.—Prone position.

position. *Fig. 3* is a film made in the upright position, showing the disappearance of the hernia as the stomach slips back below the diaphragm.

Case 11.—Mrs. R. L., a white woman, 74 years old, of the full sthenic habitus, for many years had complained of severe constipation and recently she had been troubled with a disturbing fullness in the epigastric area with dyspnea. This was always worse after a full meal. No gastric analysis was done. Blood count showed hemoglobin 80 per cent and red blood count 4,220,000. A gastro-intestinal x-ray study revealed a large esophageal hernia, about two-thirds of the fundus being herniated through the esophageal opening. A spastic colon with diverticulosis was also found. *Fig. 4* shows this large hernia, which was constant with the patient in both the upright and prone positions.

Case 17.—Miss R. H., a white woman, 68 years old, of a hyposthenic habitus, is of interest because she was examined about six months before we saw her by an excellent gastroenterologist, and after x-ray examination his diagnosis was spastic colon. She gave a history to us of filling rapidly with food, and feeling a stuffiness in the epigastric region. There was a tendency to regurgitate a mouthful of food if she lay down after a meal. A clinical diagnosis of hiatus hernia and spastic constipation was made, x-ray examination revealing in addition to the spastic colon an esophageal hernia about the size of a small orange. *Fig. 5* shows this hernia, the film being made in the prone position. *Fig. 6*, made with the patient in the upright position, shows the return of the herniated portion of the stomach into the abdominal cavity.

Case 20.—Mrs. S. E., a white woman, 74 years old, of the full sthenic habitus, presented symptoms suggesting angina pectoris. Since an attack of pneumonia 5 months before she presented herself for examination, she complained of severe "tearing pains" high in the mid-epigastrium and into the low sternal area. These pains radiated to both sides, tended to be relieved by food, and were not associated with effort or emotional upsets. With the onset of the pain, dyspnea was a marked complaint. Hypertensive cardiovascular disease of the arteriosclerotic type was present. X-ray revealed an

Fig. 4, Case 11
Mrs. R. L.—In prone and upright position. Large hernia present.

Fig. 3, Case 9
Mrs. W. K.—Upright position. No hernia showing.

Fig. 5, Case 17
Miss R. H.—In prone position.

Fig. 6, Case 17
Miss R. H.—In upright position. No hernia.

Fig. 7, Case 20
Mrs. S. E.—In prone position.

esophageal hiatus hernia the size of a large lemon, with a central contractual deformity the result of spasm or a gastric ulcer. A duodenal diverticulum and multiple gallstones were also found. *Fig. 7* shows the hernia in the prone position, but the diverticulum and gallstones are not seen on this film.

Case 24.—H. T., a white man, 41 years old, of the full sthenic habitus, complained of stomach trouble extending over a period of fifteen years. This consisted of regurgitation and substernal burning occurring after meals, made worse by carbonated drinks, alcohol, smoking and lying down. Relief was experienced by abstinence and by assumption of the sitting position. A gastro-intestinal x-ray revealed a simple catarrhal colitis and with the patient in the prone position a herniation of the stomach through the esophageal hiatus was seen. *Fig. 8* shows this hernia, and the presence of a typical gastric mucosal pattern can be seen in the herniated portion. *Fig. 9*, made with the patient in the upright position, shows the return of the herniated portion of the stomach into the abdominal cavity.

We have had none of our cases operated upon, so that we outline only the medical management, as we have advised our patients. It is agreed that surgery should be employed in some cases, and Harrington's[13] suggestions, to which we subscribe, can be followed. He says:

"From the standpoint of treatment, cases of hiatus hernia may be divided into three groups: in the first group the hernia is small and is recognized roentgenologically, often during the course of a general examination, and causes few or no clinical symptoms. The second group includes those cases in which the symptoms are moderate, and the hernias are of moderate size; in many of the cases in this group, conservative treatment such as regulation of the diet and reduction in weight is sufficient to relieve the symptoms. The third group includes those cases in which there is no response to conservative measures; in these cases the hernias are usually large, and in many cases there are complications such as incarceration of the stomach or gastric erosion. In this group of cases, the only treatment that assures relief of symptoms is operative repair of the hernia."

Interruption of the phrenic nerve, producing either a temporary or permanent paralysis of the diaphragm, is a surgical procedure that entails little risk to the patient. When radical cure of the hernia is prevented because of the condition of the patient, this is the only surgical measure which may be employed. In 185 radical repairs of defects in the diaphragm, Harrington[13] did a preliminary interruption of the phrenic nerve in 105 cases. In 25 others this was the only procedure employed.

Medical treatment varies with the individual case and is largely symptomatic. The diet consists of a bland high vitamin type, and the amount at each of the four to six feedings is small. Feedings before bedtime are not given and the patients are advised not to lie down immediately after meals. If some fullness is complained of after eating, they are advised to walk about for a few minutes. Sleeping with the upper part of the body at an angle of forty-five degrees has been found beneficial. The use of tight abdominal bands is avoided and physical exercises and deep breathing which are frequently indulged in by the athletic-minded are discouraged. As spastic constipation has nearly always been an accompanying finding in our cases of esophageal herniae, relief of this condition has been achieved symptomatically by the use of

Fig. 8, Case 24
H. T.—In prone position. Gastric mucosal pattern shows in hernia.

Fig. 9, Case 24
H. T.—Upright position. No hernia.

simple lubricants of the intestinal tract, together with antispasmodic drugs. Particular stress is laid on the necessity of not straining at stool. If anemia is present, this is treated by appropriate methods. Transfusions of blood are given if the anemia is severe, otherwise iron is given in any of the many useful forms available, as well as vitamin B complex. We have experienced gratifying results in cases showing gastric or intestinal irritative symptoms by the employment of equal parts of bismuth subnitrate and bismuth subcarbonate, in teaspoonful doses, in about one-fourth glass of water, thirty minutes before eating.

We have found the psychic factor to be a most important consideration in the treatment of our patients. Great mental distress may be produced in susceptible individuals if too much emphasis is placed upon a condition which can be symptomatically treated only, rather than radically cured. We have stressed in our cases the effect of treatment of the associated findings, such as spastic constipation, rather than directing the patient's attention to his physical defect. This indirect method of treatment has, we believe, saved some of our patients from developing a true neurosis, and it has made it definitely easier and more agreeable for us to treat these patients.

This brief review shows that the condition of esophageal hiatus hernia is not uncommon, and when kept in mind during the examination of patients will be found in from 2 to 3 per cent of all cases x-rayed. The diagnosis is only made definite by the use of the x-ray and we have found that the examination is most satisfactory when made in the prone position through the right anterior oblique angle. The symptoms presented may be cardiac, respiratory, gastro-intestinal or constitutional. Associated disorders in other parts of the gastro-intestinal tract are frequently found in cases showing an esophageal hernia and may be of more importance than the hernia. Treatment may be surgical, but medical treatment, which is largely symptomatic, has proven satisfactory in nearly all our cases.

BIBLIOGRAPHY

1. Harrington, S. W.: Jour. Thoracic Surg., **8**:125 (Dec.) 1938.
2. Carman, R. D.; and Fineman, S.: Radiology, **3**:26-45 (July) 1924.
3. Knothe, quoted by Eisen, D.: Canad. Med. Jour., **39**:207-13 (Sept.) 1938.
4. Akerlund, A.: Ibid.
5. Ritvo, M.: J.A.M.A., **94**:15 (Jan. 4) 1929.
6. Root, J. E.; Pritchett, C. P.; and Clark, P.: Cleveland Clinical Quarterly, **5**:203 (July) 1938.
7. Eisen, David: Canad. Med. Jour., **39**:207-213 (Sept.) 1938.
8. Kantor, Jno. L.: Synopsis of Digestive Diseases, p. 80. St. Louis: C. V. Mosby Co., 1937.
9. Shiro, H. C.; and Benjamin, J. E.: Ohio State Jour. Med., **36**:164-166 (Feb.) 1940.
10. Bock, A. V.; Dulin, J. W.; and Brooke, P. A.: New Eng. Jour. Med., **209**:615-625 (Sept.) 1933.
11. Ernstene, A. C.; and McGurl, F. J.: Cleveland Clinic Quarterly, **7**:209-213 (July) 1940.
12. Winans, H. M.: Tex. State Jour. Med., **34**:422-423 (Oct.) 1938.
13. Harrington, S. W.: Calif. & West. Med., **51**:27 (July) 1939.

1215 Walker Avenue

A CLINICOPATHOLOGIC DISCUSSION OF HYPERPLASTIC LESIONS OF THE URINARY TRACT*

By W. CALHOUN STIRLING, M.D.

and

J. E. ASH, M.D.

Washington, D. C.

In a previous paper we[1] gave a detailed pathologic description of proliferative lesions of the urinary tract. This paper is limited in general to a discussion of the clinical findings in such conditions.

Hyperplastic or proliferative disease of the urinary tract is of interest to the urologist because hematuria and dysuria are frequent, the probability of a cure uncertain and the possibility of metaplastic changes to malignant ones is recognized.

The incidence is much higher than a review of the literature would indicate. Hyperplastic lesions are common findings in tumors of the bladder submitted for diagnosis to the Bladder Tumor Registry.

CLASSIFICATION

Prior to Hinman's[2] classification, little attempt was made to differentiate the various forms of hyperplastic lesions of the urogenital system. Some writers still list all types under the heading of pyelitis, ureteritis, cystitis or urethritis cystica and/or follicularis, despite the fact that involvement of only a single portion of the urinary tract, other than the bladder, is uncommon. The tendency to group them under a single heading, such as "cystitis cystica," does not conform to the pathologic findings, nor does it present the true clinical picture. Six distinct hyperplastic lesions have been found and classified. We[1] added and described for the first time a lesion, not previously listed in this category, which we designated "papillary hyperplasia." The mucosa of the bladder is thrown up into blunt papillae by edema, chronic exudate and/or granulation tissue (*Fig. 8 D*). Papillary hyperplasia includes one or more features of the other groups, especially the follicular lesion, and is important because it may simulate tumor. Each lesion presents distinct characteristics from a clinical, as well as microscopic, examination, and may be found alone or in combination with other hyperplastic lesions. The point has not been previously emphasized. In three instances we found cystitis glandularis and tumor of the bladder concomitant.

Follicular lesions may develop in the presence of any prolonged infection, and probably are of little specific importance.[3] Metaplasia of bladder epithelium is not always caused by inflammation. There may be a heteromorphous occurrence of cylindrical epithelium in the wall of the bladder and development of adenocarcinoma. These various lesions may develop rapidly. A patient was observed to develop follicular cysts within thirty days.

Despite our ability to eradicate the accompanying infection, several of our patients have continued to complain of bleeding, pain and frequency of urination.

GENESIS OF CYSTS

The apparent isolation of cell nests in the submucosa of the bladder is owing to the plane in which the histologic sections are cut, and if serial sections are made through a "nest," the true relationship with the surface epithelium can be demonstrated. The lumen of the cyst is not the result of degeneration of central cells as was formerly thought, but is owing to invagination of surface epithelium. Some of the cysts are caused by a long-standing, low grade inflammatory process and may be accentuated by mechanical factors, such as stone, cystocele or prostatic obstruction. Quinby[4] says that these cysts may result from interference with the lymphatic drainage of the floor of the bladder. We did not find vesical or renal calculus in any of our patients, however, but did find three patients had prostatic hyperplasia and two cystocele and rectocele in addition to the cysts. Three other patients had a supravaginal hysterectomy performed prior to our study.

RELATIONSHIP TO CARCINOMA

It is not unusual to find leukoplakia and cystic or glandular cystitis concomitant, and this occurred in two instances in our series. Leukoplakia is of interest to the urologist owing to the possible development of squamous carcinoma. Stoerck[5] has traced a definite relation between cystitis cystica and its forerunners with multiple papilloma. Cahen[6] reported cases of cystitis cystica developing into carcinoma, and Ewing[7] observed,

*Read in Section on Urology, Southern Medical Association, Thirty-Fourth Annual Meeting, Louisville, Kentucky, November 12-15, 1940.

"one case in which a large portion of the bladder was the seat of low, nodular and cystic outgrowths from many points of which carcinoma had developed. The great majority of bladder cancers can be traced to previous or coexistent cystitis. The multiple tendency of villous carcinoma and the heterotopic recurrences indicate the existence of widespread lesions in the mucosa from which tumors may develop."

Cystic cystitis represents a later stage in the development of glandular cystitis. The cystic lesion later forms from retention of material secreted by the epithelium. In embryonal life, epithelial cells have the potentiality to form different kinds of epithelium and in basal cells this property is not lost. Some potentialities become recessive, others predominant. The law of genetic restriction is true of transitional epithelium of the bladder as it sometimes undergoes metaplasia, forming squamous cells, at other times columnar or cuboidal epithelium, and thus differentiates to the point where it actually secretes mucus.

"Adenomatoid hyperplasia is common in inflammation of mucous membrane, affects both glands and stroma, the former becoming cystic, the latter showing perivascular infiltration by lymphocytes. This may produce edema, venous stasis and mechanical traction, leading to papillary and polypoid outgrowth with a striking tendency toward development of malignant adenoma and carcinoma." (Ewing[7]).

Our first clinical case, an infiltrating carcinoma, Grade III, was found to have cystitis glandularis in association with the new growth.

Mr. L. P., aged 37, seen April 22, 1936, complained of severe pain in the bladder area and frequency of urination. Cystoscopic examination showed a bladder capacity of 180 c. c. with definite hypertrophy of the trigon, which was covered by small elevated nodules down to the vesical orifice. There was no interureteral hypertrophy, but a definite median bar was present.

The upper portion of the urinary tract on retrograde pyelography showed no evidence of disease. A culture of the urine from the kidneys showed *coli* infection. Cystoscopy showed cystitis glandularis. These areas were mildly fulgurated several times. The infection completely subsided, but the frequency of urination continued and a passage of blood was noted. A cystoscopic examination six months later showed the entire trigon and an area extending to the left lateral wall of the bladder studded with papillary projections. It did not resemble bulbous edema. Biopsies revealed an infiltrating carcinoma of the bladder, Grade II. Leukoplakia of the trigon was also noted. Owing to the size and position of the neoplasm, the bladder was opened, the tumor destroyed and the base irradiated with radon seed. Cystoscopic examinations at intervals of six months showed no recurrence of the neoplasm.

Fig. 1
Bilateral retrograde pyelogram showing early dilatation of renal pelves, narrowing of infundibula and mottling of ureter caused by pyelo-uretero cystitis glandularis.

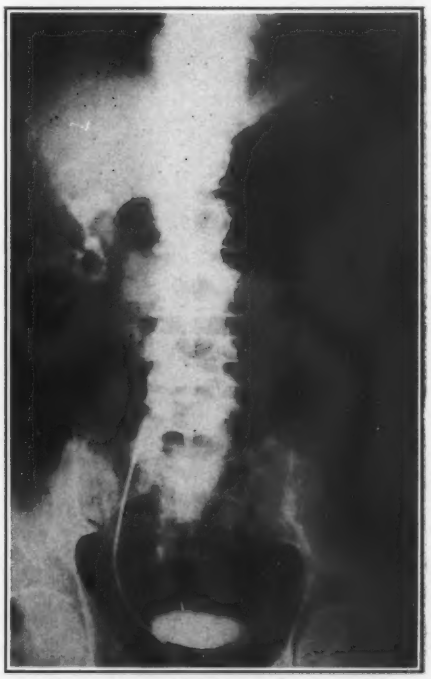


Fig. 2
Retrograde pyelogram right kidney showing narrowing of infundibula with calical dilatation and filling defects in lower portion of the right ureter and bladder from glandular metaplasia. Left kidney congenitally absent.

The second patient had papillary carcinoma of the bladder, associated with cystitis glandularis.

Mr. J. T. M., aged 26, examined September 28, 1932, had pain and frequent urination with hematuria for six months. Cystoscopic examination revealed a small, red papillary mass lateral to the right ureteral orifice. The bladder wall was not invaded. The tumor was removed by fulguration and showed papillary carcinoma, Grade II. Subsequent examinations showed no evidence of recurrence until the same symptoms were noted three years later. A small papillary tumor slightly lower and medial to the right ureteral orifice was found. It was removed by fulguration and sections showed the same type of tumor found at the first examination. The bladder was free from tumor until two years later, when a third tumor was found superior and medial to the left ureteral orifice. It was red, bleeding and necrotic in places. The tumor was removed with the resectoscope and showed papillary carcinoma, Grade II. The bladder wall was slightly edematous and the tumor showed some tendency to invade the bladder wall. The mucosa around the tumor contained several small nodules resembling glandular cystitis. Biopsies of these confirmed the cystoscopic diagnosis. During the interim he developed calculi in his left kidney and spontaneously expelled several small stones. Culture of the urine showed *Bacillus coli*, staphylococcus, and *Streptococcus hemolyticus*. No acid-fast organisms were found, although the right kidney had been removed ten years ago for tuberculosis. Subsequent cystoscopic examination has shown no evidence of recurrence of the tumor.

Fig. 3

Bilateral retrograde pyelogram showing mottling of renal pelves from pyelitis cystica. Note irregular dilatation of ureters from same cause.

Inasmuch as three tumors were found in different portions of the bladder, their presence does not represent a failure to arrest the growth of the tumor, but does represent some imponderable factor present in the bladder of this patient capable of producing metaplastic changes of a malignant nature.

A third patient showing malignant changes with glandular cystitis was Mrs. L. R. C., aged 66. There was hematuria, pain, and frequency of unrination. Six years ago she had similar symptoms, including hematuria. A tumor was found and removed by open operation. She had no further trouble until the present attack began. An intravenous pyelogram showed suspicious filling defects in both ureters and renal pelves (*Fig. 3*). Spheric dilatation of the pelvis could not be found, and the minor calices were not distorted. Characteristic mottling could be seen in the lower portion of both ureters. Culture of the urine showed *coli* and *staphylococci*. Four or five pearly gray cysts were seen lateral to the left ureteral orifice. Some nodules resembling cystitis glandularis were seen near the right ureteral orifice. Biopsies from both areas confirmed the cystoscopic diagnosis. The cysts were fulgurated and the patient is entirely free of symptoms after one year.

COMMENT

Three cases are presented in which a tumor was found associated with cystitis glandularis. These findings confirm the observation of Ewing[7] and Patch[8] as well as our own, that cystic lesions of the urinary tract may and do undergo malignant degeneration.

There seems little doubt that inflammation plays a part in producing these cysts, but what additional factor determines the type of metaplasia is certainly not clear. It does seem that there must be some general influence causing it other than an inflammatory one. It might be vitamin A deficiency in the case of stratified squamous epithelial metaplasia.

It is not uncommon to find large areas of the urethra or bladder mucosa thrown into low folds accompanied by glandular metaplasia of the epithelium. In this instance gland-like structures, even large branching ones, are seen deeply embedded in the stroma. This description represents the pathologic picture of glandular cystitis. These points are illustrated by the histologic section seen in *Fig. 7 B*. Some of these cysts have been cut in cross section, being isolated

"glands" (glandular cystitis) and "nests" (Brunn nodule) formed in the subepithelial stroma. All of these, however, are connected with the surface epithelium. The Brunn nodule or "epithelial nest" represents the blind end of a crypt and is not an isolated nest, as was formerly thought to be the case.

SYMPTOMS

Hyperplastic disease of the urogenital tract presents no pathognomonic symptoms. The cysts are usually found in older individuals, and women are more prone to develop them than men (3 to 1).

Hematuria is the most characteristic symptom, often being associated with dysuria and frequency of urination, as every patient in this series had one or more of these symptoms. The vesical tenesmus is very difficult to control and is as severe as that found in tuberculous cystitis. Pain over the bladder area is a common finding. The capacity of the bladder is not lessened. Hyperplastic changes should always be considered if other causes for hematuria can be eliminated.

DIAGNOSIS

The roentgen ray study of a typical case of hyperplastic disease with renal involvement would show dilatation of the terminal calices, narrowing of the infundibula and spheric dilatation of the pelvis of the kidney. Cystic dilatation of the ureteropelvic junction (not a true pyelectasis) is typical of pyelitis cystica (Hinman[2]). Filling defects, dilatation, tortuosity or constriction of the lumen of the ureter occur from the presence of cysts in the wall.

On cystoscopic examination it is not easy to distinguish between cystitis cystica, follicularis and glandularis. Cystitis cystica, however (*Fig. 11*), can usually be recognized by the regular, rounded, sharply circumscribed and pearly appearance of the cysts, the total number being less than that found in cystitis follicularis. If the diagnosis of cystitis cystica is verified by positive biopsy, a bilateral pyelo-ureterogram should always be made. In cystitis follicularis the mucosa of the bladder (*Fig. 12 A*) is covered with nodules of varying size, rather closely packed together, of greyish-red color and firm on pressure. They are best seen with the McCarthy foroblique cystoscope with the bladder but partially distended. Follicular or granular lesions of the urethra are well outlined by this technic.

Fig. 4

Whole biopsy specimen removed from bladder showing cystitis follicularis, three germinal centers present. X represents forceps bite.

Fig. 5

Whole biopsy specimen from bladder showing: (A) cystitis follicularis; (B) cystitis glandularis; (C) cystitis cystica, a later stage of cystitis glandularis. Note metaplasia of epithelium.

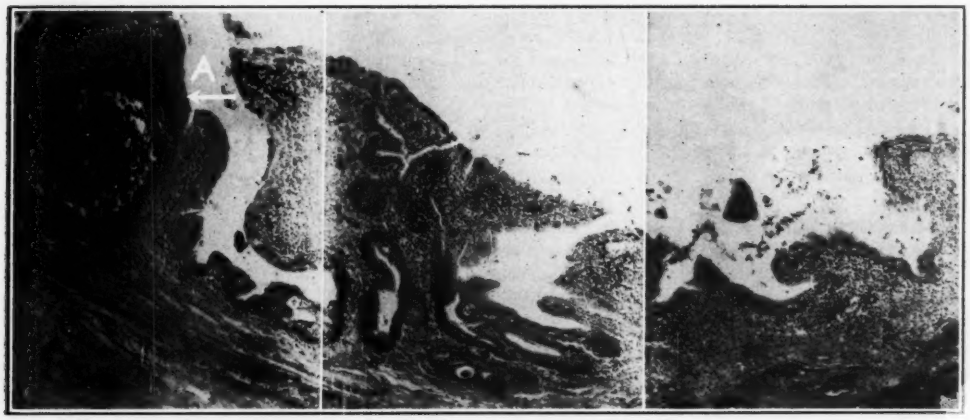


Fig. 6 Fig. 7 Fig. 8

Six contiguous sections of single portion of anterior bladder wall adjacent to papillary carcinoma showing successive changes in epithelium. (A) represents cystitis follicularis (Fig. 6); (B) cystitis glandularis (Figs. 7 and 9); (C) columnar metaplasia (Fig. 7); (D) papillary hyperplasia (Fig. 8); (E) cystitis cystica (wall collapsed) (Fig. 11).

Glandular cystitis (*Fig. 8*) presents irregular, mammillated elevations, confined chiefly to the neck and trigon of the bladder. We have also found them in the dome or anterior surface of the bladder. Cystitis granulosa is seen as a cluster-like arrangement of granulation tissue and may be hemorrhagic from ulceration and simulate a tumor on cystoscopic examination. A biopsy should always be made of any nodule or cyst found in the bladder and will, no doubt, disclose a greater incidence of cysts than is now thought to be the case. Tuberculosis, tumor and Bilharzia disease must be considered in the differential diagnosis.

TREATMENT

Hyperplastic pyelocystitis is very difficult to eradicate owing to involvement of the subepithelial tissues. A long period of treatment may be required to eradicate the underlying cause. Light fulguration of the entire vesical outlet has been employed and will often relieve the pain and frequency of urination. Instillation of medicated oil or a weak solution of silver nitrate, preceded by a local anesthetic, has been helpful in some cases. Roentgen rays have also been used, but have not relieved the pain nor stopped the formation of cysts.

Owing to the frequency of bilateral involvement of the renal pelves and ureters, nephroureterectomy should be reserved for cases with advanced unilateral destruction of the kidney. Two cases requiring nephrectomy were recently reported by Van Duzen and Cantrell.[9]

Focal infections, including those of the cervix uteri, must be eliminated before treatment is completed. Dilatation and light fulguration of the urethra afford considerable relief in granular, glandular or follicular urethritis. Zimmerman[10] reported three cases of follicular and glandular urethritis, one of which also had a tumor of the bladder.

ANALYSIS OF CASES

Four female and two male patients in this group of 22 had transurethral resection of median bars situated in the neck of the bladder. In 3 of these cysitits glandularis was found alone, a fourth showing a combination of follicular and glandular cystitis. One had complete retention of urine. Bilateral involvement of the ureters and pelves of the kidney was found in 5 of our cases, none of which required surgical interference. Four other female patients had either follicular, granular or glandular lesions in the urethra. In all 22 patients the clinical diagnosis was verified by histologic study. Seventeen were female, 5 male, and the average age was 60 years.

Vitamin deficiency has not been found, but one should always consider this possibility. The lesions may persist regardless of therapeutic measures and the fact that in 5 instances the urine was sterilized only later to become rein-

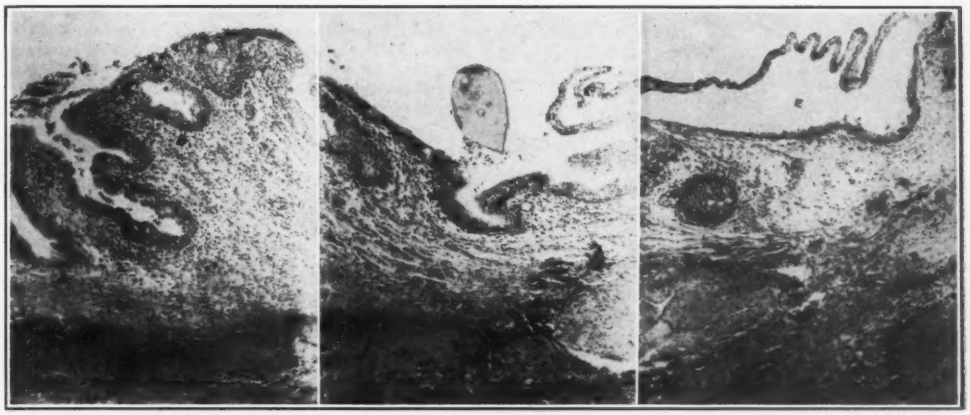


Fig. 9 Fig. 10 Fig. 11

Fig. 12
Low power section of bladder wall showing concomitant lesions of cystitis follicularis (A) and cystitis glandularis (B). (Case 3.) X 70.

fected indicates a deep-seated infection. We found, however, that the vesical symptoms tend gradually to disappear as the infection lessens. The sulfamido group of drugs has been helpful in these cases. Sulfathiazole seems to possess advantages over sulfanilamide and sulfapyridine, especially in mixed infections where staphylococcus, *Bacillus proteus* and *Streptococcus faecalis* are found. Culture has shown the colon bacillus in every patient.

SUMMARY

(1) Twenty-two cases of hyperplastic lesions of the urinary tract are reported.

(2) Either hematuria, dysuria or frequency of urination were found in every instance and were usually severe.

(3) The genesis of glands and cysts and their relation to carcinoma are discussed. Three of our patients had concomitant cysts and carcinoma of the bladder.

(4) Brunn's follicle is an invagination, or extension of surface epithelium, and its subsequent fate depends on whether the epithelial metaplasia progresses to a squamous or a glandular type.

(5) Follicular cystitis is a nonspecific entity, common in any chronic infection.

(6) Several hyperplastic forms of cystitis may be found in the bladder at the same time.

(7) We have described for the first time a lesion termed "papillary hyperplasia." It may combine one or more features of the other types and is important, as it may simulate tumor.

REFERENCES

1. Stirling, W. C.; and Ash, J. E.: Pyelitis, Ureteritis and Cystitis Cystica, Follicularis, Glandularis and Granulosa with a Note on Their Pathogenesis. Jour. Urol., **45**:381 (March) 1941.
2. Hinman, Frank: The Principles and Practice of Urology. Philadelphia: W. B. Saunders Co., 1935.
3. Stirling, W. C.: Cystitis Follicularis, with Discussion of Other Proliferative Lesions of the Bladder and Report of Cases. J.A.M.A., **112**:1326 (April 8) 1939.

4. Quinby, W. C.: Discussion, Pyelitis Ureteritis and Cystitis Cystica. Tr. New England Branch, Amer Urol. Assn., p. 48, 1938.
5. Stoerck, O.: Ztschr. f. Urol., **1**:133, 1902.
6. Cahen, V. A., cited by Ewing,[7] p. 943.
7. Ewing, James: Neoplastic Diseases, 4th Ed., pp. 942 and 943. Philadelphia: W. B. Saunders Co., 1940.
8. Patch, F. S.: Pyelitis Ureteritis and Cystitis Cystica. Tr. New England Branch, Amer. Urol. Assn., p. 48, 1938.
9. Cantrell, R. H.; and Van Duzen, R. E.: Ureteritis Cystica. Urol. & Cutan. Rev., **44**:641 (Oct.) 1940.
10. Zimmerman, I. J.: Urethritis Follicularis. Tr. New England Branch, Amer. Urol. Assn., pp. 85-92, 1939.

DISCUSSION (*Abstract*)

Dr. Jefferson C. Pennington, Nashville, Tenn.—I have followed Dr. Stirling's work ever since he began this several months ago, and I have followed to some extent other men's work, particularly Hinman. One thing that seems to be noteworthy is that all these cases show colon bacillus infection.

In spite of the fact that I have looked diligently for these cases, I have not seen one that I recognized.

Dr. T. Leon Howard, Denver, Col.—I want to impress upon you the importance of chronic infections in these cases. I have never seen a case which had not a chronic colon bacillus infection, and we treat colon bacilli too lightly in the bladder. In most cases we have obstructive substances, too. Whether you call them follicularis cystica or cystitis follicularis, all these cases indicate a chronic disease. A certain percentage will become malignant. The trouble about the whole matter is that we cannot eliminate the colon bacillus.

To me, the poorest part of American medicine today is diagnosis in the big bowel. In some of these cases x-ray and bismuth enemas will show diverticula of the bowel, and we as urologists should teach the general medical man to help us clean up these infections.

We are not using the proper cystoscope. Many of these patients are old women around 55 or 60, and we are not making enough diagnoses of retention of the ureter in them. If they urinate before they get on the table, we frequently find two or three ounces of urine still in the bladder. If we inject olive oil or liquid vaseline into the bladder, a week later we may find the same vaseline there. If they cannot empty the vaseline, they cannot empty the urine. Until we get rid of the residue, we shall not cure these cases, and we are curing only a few of them.

In my opinion, we are not fulgurating them deeply enough. If we run the cystoscope over these cysts, we frequently will squeeze out a milky mucous membrane.

Dr. Harry M. Spence, Dallas, Tex.—I should like to ask Dr. Stirling what his feeling is about the relation of cystitis glandularis to the cystic lesions of the urethra that we see in women commonly. I have in mind a woman of approximately 70 who had been seen for about five years, off and on, by Dr. Harold O'Brien and me. We did innumerable pelvic examinations and frequent cystoscopic examinations, finding always granular and cystic lesions. While she was under observation, she developed a very fulminating, infiltrating carcinoma of the urethra, which terminated fatally.

Dr. C. P. Segard, Leonia, N. J.—A number of cases of colon bacillus infection of the bladder may be cured by teaching women that they wipe the wrong way. A man wipes from forward backward; a woman wipes from backward forward. Thus she carries the infection forward into the vagina and the colon bacilli work their way up. If we put a stop to that, we will have no infection from this source.

Dr. Stirling (closing).—Urology owes a good deal to Dr. Folsom, of Dallas, for calling attention to the presence of gland-like structures in the urethra. Many writers did not agree with his findings, but the work of Patch, Rhea, McKenzie, as well as our own observations, have confirmed his studies. There is no question of the presence of glands in the trigon of the bladder and urethra. We frequently find cysts, lymph follicles and other evidence of metaplastic changes in this area. Ewing, Ash, Cajigas and other pathologists have examined tissue from the urethra and found follicles, cysts and glands in the floor of the urethra and bladder. These hyperplastic lesions usually represent a low-grade inflammatory process in which the transitional epithelium of the bladder undergoes metaplasia to either a squamous or columnar type and in a number of instances undergoes malignant changes.

Colonel Ash found either follicular or glandular cystitis in quite a proportion of the cases submitted to the Bladder Tumor Registry. If we examine the urethra with the McCarthy foroblique instrument, with the bladder but partly filled, the cysts can be more easily demonstrated. If we take biopsies in all suspicious cases, we will find them to be more prevalent than the literature indicates.

EPIDERMOLYSIS BULLOSA ACQUISITA*

By JOSEPH L. HUNDLEY, M.D.
and
DUDLEY C. SMITH, M.D.
Charlottesville, Virginia

Epidermolysis bullosa is an uncommon, peculiar disorder of the skin, occurring in early life, and characterized essentially by the development of vesicles and bullae following insignificant trauma. Constitutional symptoms are lacking. It is usually hereditary. Acquired epidermolysis bullosa in the adult is sufficiently rare to render authentic cases of it worthy of record and of thorough investigative studies.

It is thought that Tillsbury Fox, in 1879, first described epidermolysis bullosa as "congenital ulceration of the skin with pemphigus eruption and arrest of development generally." Goldschneider, in 1882, accurately described this condition and called it "acantholysis bullosa." The term "epidermolysis bullosa" was first used by Koebner in 1886. Other authors reporting cases shortly afterwards were: Valentin, Torak, Blumer, El-

*Read in Section on Dermatology and Syphilology, Southern Medical Association, Thirty-Fourth Annual Meeting, Louisville, Kentucky, November 12-15, 1940.

*From the Department of Dermatology and Syphilology, University of Virginia, Charlottesville, Virginia.

liott and Kelbs. The most important later contributions have been made by Luithlen, Kablitz, Wende, Hodara, Kanoky and Sutton, Ormsby, Wise and Lautman, Henrichsbauer, Engman and Mook, Fordyce, Howard Fox, McKee, Guy, Cockayne, Tobias, Herlitz, Beinhauer, Kittredge, and Davidson.[1]

Clinically, this disease has been divided into two forms, the simple and the dystrophic. In the former, lesions occur only on the skin, the bullae healing without scars, and the syndrome often disappearing after puberty. In the dystrophic form the bullae, sometimes hemorrhagic, may occur on both the skin and mucous membranes. They often require greater traumatic provocation; on healing they leave scars and pigmentation. In addition, in this latter group the loss of hair and nails and the presence of epidermal cysts are frequent. Likewise the bullae histologically are usually seen to be deeper than those of the simple variety. Cockayne[2] subdivides the dystrophic form into three genetic classes.

The exact cause of the formation of bullae in this disease remains unknown. A number of theories have been enumerated. It has been considered essentially an acantholysis at the junction of the epidermis and papillary dermis. The formation of the bullae has been thought to be the result of sudden and excessive serous exudation in an individual with an irritability of the cutaneous vascular system.[3] Endocrine disturbances have been incriminated.[4] Improper development of the rete cells and a lack of proper trophic nerve innervation have been mentioned.[5] Some have considered the mechanism of lesion formation similar to that for urticaria. Others nonspecifically indict an inborn error of metabolism.[2] In several of the cases in which histologic studies were done deficiency of or defects in the elastic tissue of the upper derma have been noted. Engman and Mook,[6] Kanoky and Sutton,[7] and Weiss made this observation on both injured and uninjured skin in patients with epidermylosis bullosa hereditaria. Wise and Lautman,[8] however, found the uninjured skin normal in an acquired case. In some cases the elastic tissue has been found to be apparently normal, even beneath the bullae.

Although Kablitz had described "epidermolysis bullosa acquisita" in 1904, and Ormsby and others had later presented cases of posttraumatic bullous dermatoses coming on in adult life, "acquired" epidermolysis bullosa was not generally accepted in this country until 1915. In that year Wise and Lautman[8] reported the case of an Austrian male in whom bullae and epidermal cysts first appeared at the age of 39, the family history revealing no bullous skin diseases. They state that the question of hereditary transmission is entirely eliminated in this case and in Bukovsky's case as well. In the support of the argument for the existence of the acquired form of the disease, they cite the case of Engman and Mook, in which traumatic bullae were frequentely noted for years afterwards at the site of a previous severe chemical dermatitis on the hand of a plasterer. They further point out the possibility of the ingestion of arsenic as a provocative agent in increasing the vulnerability of the skin to trauma.

Since 1915 a few other cases of the adult or acquired type have been reported. McLeod (1931) described the case of a retired British colonel who, at the age of 50, suddenly developed a bullous response to the slightest pressure on his hands. Pines[10] recently presented a Polish woman of 55 who maintained that her bullous lesions had been present only six months and that none of her family or known relatives were similarly affected. Bloom and Oppenheim nevertheless agreed to call this case "epidermolysis bullosa tarda," that is hereditary with tardive or delayed manifestations.

CASE REPORT

Mr. J. S., a 75-year-old white man, was first seen in the Out-Patient Department on October 6, 1939. His complaint was an itching rash over both ankles and shins, and a similar eruption accompanied by some "blisters" over the dorsum of both hands and forearms. It was noted that he had no nails on the fingers or toes. These, he stated, had been lost 18 to 20 years previously. Adequate investigation of this case was delayed until October 31, 1939. At this time a history of posttraumatic bullous lesions of the hands and feet over the past several years was obtained. This information, coupled with the obvious loss of all nails, suggested the interesting possibility of epidermolysis bullosa of the acquired type. Admission to the hospital ward was arranged.

The patient says that the skin of his hands has always been prone to fissure following farm labor, but repeatedly insists that there were no "blisters" until he began losing his nails. The first lesion was a "blister" which appeared at the base of one fingernail 20 years ago at the age of 55 following the accidental insertion of a wood splinter at this point. As this lesion spread around the base of the nail the latter loosened and came off intact. Within the next two years the other nails of the fingers, then those of the toes, one by one, were lost by a similar relatively painless process following bleb formation in the paronychial regions. It appears that a mild injury preceded the loss of these nails. The story does not depict an infectious process.

Several years later, and in the past ten years only (the patient's age was then 65) there began to occur scattered periods of "blister" formation, chiefly on the

backs of the hands and on the toes, but occasionally on the elbow and shin regions. These lesions, which appear to have followed trauma, often mild, are frequently associated with a dermatitis of these areas. The "blisters," occasionally hemorrhagic, usually heal rapidly, leaving only a faint scar. Constitutional symptoms are usually lacking. There should be noted the patient's statement that in the past five years the skin of his hands and feet has become "as thin as tissue paper." He denies any summer or seasonal increase of the bullae and denies hyperhidrosis as well.

This man's general health has always been good. The past few years have brought some symptoms of cardiovascular disease and occasional severe chest colds. He has good habits, getting regular hours of sleep and using no alcohol, tobacco, or drugs. His diet is apparently adequate. He is a general farmer.

The family history is interesting because of consanguinity, but it fails to uncover any similar skin disorder. The patient's father and mother and both grandfathers as well as his maternal grandmother were named Shiflett. There are numerous incidences of consanguinity among these people. The patient is the youngest of five children, all of whom are still living, ages ranging from 75 to 81 years. There were 8 siblings in his father's family, 9 in his mother's. The patient has 8 children, one dead at 18. He states positively that there have been no comparable or serious skin disorders in any member of his family, including parents, grandparents, uncles, aunts, siblings or children.

On physical examination this man is seen to be well developed, nourished and preserved. He has about 25 per cent the normal amount of grayish hair on the scalp. The anterior surface of the lower legs and ankles is mottled with erythema ab igne and with a mild, dry, scaly dermatitis. A few petechiae are seen on the ankles and scrotum. All the nails of the fingers and toes, except for a 5 mm. sized piece on the fourth digit of the left hand, are absent, leaving a smooth, shiny, skin-covered bed. Most of the teeth are missing, the remainder carious. The aortic second sound is slightly accentuated and the blood pressure is 170/100. A few moist rales are heard in the bases of both lungs. The abdomen is somewhat obese, the genitalia are normal. The ear, nose, throat and lymph nodes are essentially negative. A low-grade generalized arteriosclerosis is evident from examination of the optic fundi and peripheral vessels. The prostate is somewhat hypertrophied. Several of the deep reflexes are absent. The skin appears to be dry, and over the dorsum of the hands and fingers, feet and toes, elbows, knees and shins it is rather thin. No vesicular or bullous lesions are now seen, but over the above areas there are several thin, erythematous, faint scars. No epidermal cysts or lesions of the mucous membrane can be found, nor is there any hyperhidrosis. Dermatographism is absent.

Urinalysis, blood counts and differential smears, platelets, bleeding time, and coagulation time are all within the limits of normal. The tourniquet test produced no petechiae. Analysis of the gastric contents revealed nothing abnormal. A urine culture for typhoid bacilli is reported negative, as are the Wassermann and Kahn serologic tests. The basal metabolic rate, thought to have been made under unsatisfactory conditions, is reported as plus 24 per cent. Tests for porphyrin in the urine are reported negative.

On this admission no definite diagnosis or specific treatment was given. On November 24, 1939, the patient returned, presenting several small rather tense bullae on the left thumb, filled with clear serum. There was also a small hemorrhagic lesion in the nail bed of the left thumb. A biopsy was taken through a bleb on the hand and through the site of a recently healed lesion above the right knee.

Fig. 1
Bullae of the thumb.

Fig. 2
Bulla on the ring finger.

A week later all bullae were healed and Fowler's solution was prescribed. Five weeks later the patient had recovered from a severe chest cold and from two small "blisters" on the feet. A biopsy was taken from apparently normal skin of the right flank.

The next visit, six weeks later, March 14, 1940, revealed several irregular thin-walled bullae on the dorsal surface of some toes, including the nail beds, and a particularly large, clear, tense one on the flexor surface of the right ring finger. The latter lesion followed within a few hours the tying of berry vines with a cord two weeks previously. The patient was given 30 drops of oil of percomorph daily.

He was seen for the last time on May 14, 1940. Several "blisters" had occurred on the hands and feet in the two-month interval. There were then present a pea-sized bleb of the right hand, a tremendous bulla of the right second toe, and a smaller one of the left second toe. The patient had recently been pushing a lawn mower. The hand lesion was excised *in toto* for histological preparation.

A recent message from his daughter states that Mr. J. S. died on June 5, 1940, of "heart trouble."

HISTOPATHOLOGY

Specimen 1 is a bulla excised *in toto* from the ulnar aspect of the right hand.

Grossly and under the reversed ocular there is visible a large vesicle, 1 cm. in length, occupying the center of the section. The vesicle is filled with pinkish gray material containing a very few red and white blood cells, and it is situated between the malpighian layer and the stratum corium. The latter is decidedly hyperkeratotic. The granular layer is thick everywhere, but especially beneath the vesicle. The rete shows moderate acanthosis, which becomes marked beneath this lesion. There is also a moderate amount of intercellular edema in this portion of the rete.

The subpapillary layer and to a lesser extent the deeper portion shows a rather marked basophilic degeneration. This is more marked subjacent to the bulla. There is here seen a moderate amount of perivascular round cell infiltration containing an occasional polymorphonuclear leukocyte. A moderate amount of intercellular edema involves these same areas. The sweat and sebaceous glands show some atrophy. No epithelial cysts are seen.

Elastic tissue stains (Weigert's and van Gieson's) show the degenerated tissue of the corium to be collastin. Elastic fibers are much decreased in the papillary corium, particularly beneath the bulla, where no fretwork of fibrils joining this layer with the basal cell layer can be found. In the deep portions of the corium the elastic fibers are seen to be partially fragmented and coarsened.

Specimen 2 is an ellipse of skin through a scar on the right suprapatellar region.

This section shows changes which are characteristic of so-called senile atrophy, with a definite but less marked deficiency of elastic fibers in the papillary corium. Definite hyperkeratosis, acanthosis and inflammation are lacking. No cysts are seen.

Specimen 3 is an ellipse of unaffected skin from the right flank.

In this specimen only changes consistent with senility are seen. There is little or no degeneration in the corium and no changes except thinning in the epidermis. The striking feature, in contrast to the above sections,

Fig. 3
Bullous lesions on the toes and dermatitis of the feet.

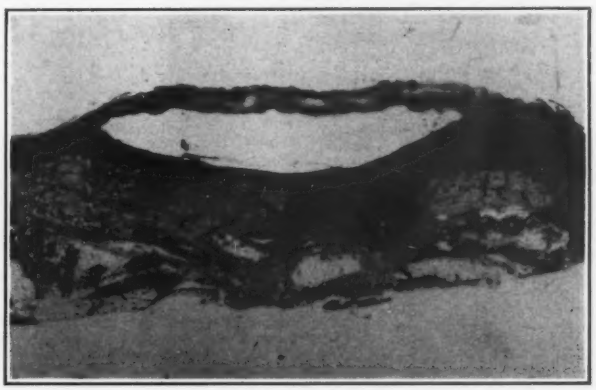


Fig. 4
Section through a bulla (x5).

is the presence of a definite network of elastic fibrils joining the papillary layer of the corium to the basal cell layer of the epidermis. Only a slight decrease in amount and a slight fragmentation of elastic fibers is noted, this being in the upper corium.

COMMENT

That this case falls into the epidermolysis bullosa group there can be little doubt. The relationship of the bullous lesions to trauma is at least reasonably clear throughout the course of this disorder, and at no time was there evidence of associated acute constitutional disease. It is believed, from the history, that the loss of the nails resulted not from a local infectious process, but from dissecting bullous lesions of the nail beds resulting from trauma. The bullae themselves occurred only on sites particularly exposed to trauma. Clinically and histologically, there is evidence of only slight inflammation in these lesions, a picture which, incidentally, is consistent with that of pemphigus vulgaris. The latter disease is eliminated in this case by a lack of constitutional disturbances, by the absence of spontaneous blebs, by the occurrence of distinct areas of predilection, and by the presence of scars at the sites of pre-existing bullae. Dermatitis herpetiformis is eliminated by the same reasons and by the absence of marked pruritus, of wheals, papules and pigmentation. Bullous drug eruptions are likewise eliminated by the history. Porphyrinuria congenita need scarcely be mentioned; exposure to sunlight has been specifically acquitted of a causative relationship by this man and tests for porphyrin in the urine have been negative.

Clinically, because of loss of the nails, this case presents some of the features of the dystrophic type. Histologically, however, because the bullae are superficial in the epidermis, one would group it in the simplex variety. We are forced to classify it as of the mixed type.

The most notable feature of this case is the advanced age of the patient (about 55) at the time of onset of his lesions. The development of the lesions of epidermolysis bullosa after the age of 50 must be exceedingly rare. An isolated and somewhat doubtful case in which the onset of bullae occurred at the age of 73 has been reported.[8] The great majority of the other reported cases are of individuals under 50. We wish, at this point, to express the thought that it is difficult to imagine an "inborn" error of this kind remaining latent for over fifty years, especially in a laborer. To call this and other similar cases "tardive" supposes a set of circumstances in which the predisposing or formal factor is not active in the presence of the ubiquitous exciting factor (trauma) until relatively late in life. It would seem more logical to label these adult-life cases "acquired." The conviction that this is truly an acquired case is strengthened by the absence of a history of suggestive skin lesions in the family, the pedigree being reasonably clear as remotely as the great grandparents. The his-

Fig. 5
Bulla from the hand, low magnification (hematoxylin and eosin stain).

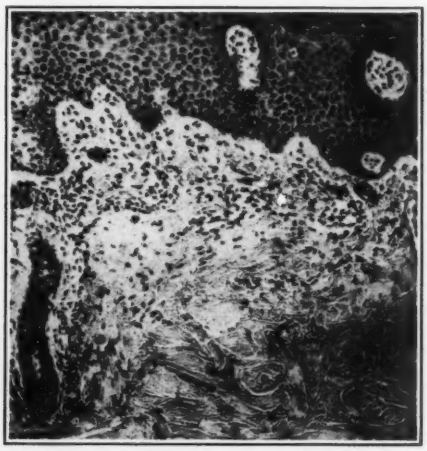


Fig. 6
Subjacent to bulla from hand, moderate magnification (hematoxylin and eosin stain).

tory of consanguinity does not alter the facts of the case.

The concept of a formal and a causal factor is of course not new in medicine. The etiology of most diseases is related to both predisposing and exciting factors. In the case of cancer particularly it is thought that both factors, termed formal and causal, must be operating before the individual develops a malignancy. In the case of epidermolysis bullosa the causal factor (trauma) is so universally present that one would expect the lesions to develop quite early in life. The fact that there are cases developing only in adult life indicates that the basic or formal factor may be acquired. One cannot deny, of course, that a course of events somewhat analogous to those in cancer may take place in these so-called acquired cases; and in spite of the presence of the formal and, to a lesser degree, the causal factors throughout life, lesions rarely develop until relatively late. We feel that senile degeneration of supporting structures in the skin predisposes to the acquired form by rendering the skin more vulnerable to trauma. It is possible that malnutrition, avitaminosis, toxemia, infection, angioneurosis or trophoneurosis may play some role in these cases. If that be true, an hereditary factor may not necessarily be present in the "acquired" cases.

Fig. 7
Normal skin from the flank area. Note the elastic fibrils in the papillary corium (elastic stain, Weigert's and van Gieson's).

In the final analysis it is doubtful that epidermolysis bullosa, congenital or acquired, is a distinct clinical entity. Referring to the hereditary form, Cockayne[2] divides the cases into several genetic groups, and states that there is probably a group of closely related conditions included under this term. Wise and Sulzburger[11]

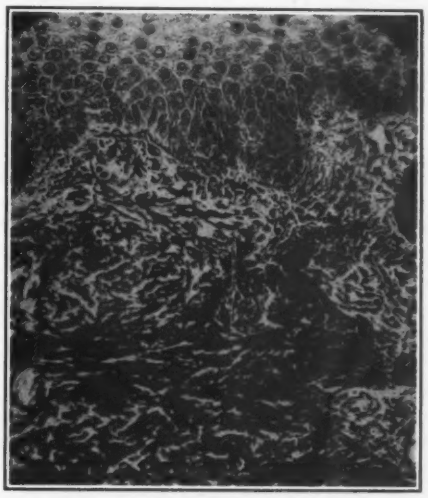


Fig. 8
An area subjacent to a bulla on the hand. Note the deficiency of elastic fibers in the papillary corium and basophilic degeneration of collastin (elastic stain, Weigert's and van Gieson's).

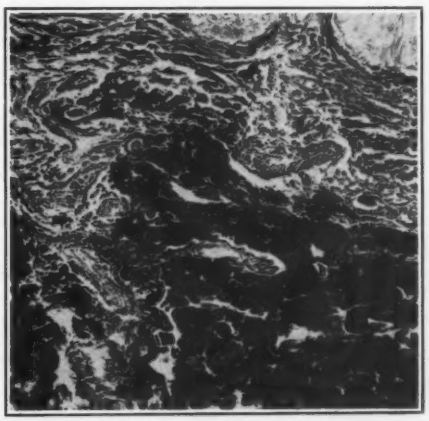


Fig. 9
Area beneath a bulla of the hand. Note the deficiency of elastic fibers in the papillary corium and degeneration of the collastin throughout (elastic tissue stain, Weigert's and van Gieson's).

suggest the possible close relationship of "familial benign chronic pemphigus" of Hailey and Hailey, "keratosis follicularis (Darier) with vesiculation" of Pels and Goodman, "recurrent herpetiform dermatitis repens" of Ayres and Anderson, and "dyskeratosis vesicularis hereditaria" of Rein and Frank to epidermolysis bullosa hereditaria. Some cases of the latter syndrome undoubtedly simulate a closely congenital ectodermal defect as well as porphyrinuria congenita. As concerns the acquired form, Wise and Lautman found it difficult to distinguish chronic benign pemphigus, and suggested that there may be transition forms. The notable variations in the location of the bullae, in the amounts and character of the elastic tissue, and in the clinical course of the disorder indicate that all cases cannot be accounted for by the same mechanism.

The deficiency and fragmentation of elastic tissue beneath the bullae, as shown in the sections, supports the theory of etiology first championed by Engman and Mook.[6] The significance of these findings we do not profess to know, but the prolongation of the elastic fibrils, absent here, is thought to help bind the epidermis to the corium. One wonders why deficiency of elastic tissue and collastin is more marked beneath the bullae than in the immediately adjacent skin. Why is it more marked under a fresh bulla than under the site of a pre-existing one? Why is this degeneration so much more marked in the skin over the extremities than that of the flank? Is this a case of degeneration of elastic tissue limited to the extremities? It is possible that the picture is simply that of sailor's or farmer's skin (senile atrophy). If the loss of supporting tissue is considerable, as in this case, it is obvious that the skin is more vulnerable to injury to which it may react with the production of a bleb or bulla. In that sense these lesions, if so produced, and resulting indirectly from acquired changes in the skin, represent an acquired form of epidermolysis bullosa.

The mechanism by which trauma stimulates the formation of a vesicle or bulla is not understood. Does it act directly on the cells themselves, on the nerve endings, on the blood or lymph supply, or does it intensify the action of a toxic agent? The phenomenon of dermatographism comes to mind, but with the limits of present knowledge a satisfactory explanation cannot be given.

SUMMARY

Epidermolysis bullosa is defined and classified. A brief review of the literature is incorporated.

The theories of etiology of various authors are stated.

A case report is given of a man in whom the lesions first appeared at the age of 55 and continued until the age of 75, and in whose family there have been no similar skin disorders. Histologic study shows the collastin and elastic fibers to be markedly degenerated and deficient beneath the bullae, but not in unaffected skin from the flank.

In the comment the views of possible etiologic relationship are presented. The differential diagnosis is briefly discussed. The case is classified in the mixed (simple-dystrophic) group. It is thought to be a truly acquired case of epidermolysis bullosa.

Epidermolysis bullosa, hereditary or acquired, is a syndrome and probably not a distinct clinical entity.

The mechanism of the formation of bullae by trauma is not understood.

BIBLIOGRAPHY

1. Davidson: Amer. Jour. Dis. Children, **59**:371 (Feb.) 1940.
2. Cockayne: Inherited Abnormalities of the Skin. London: Humphrey Milford, 1933.
3. Elliott: Jour. Cut. Dis., **23**:10, 1895.
4. Guy: Arch. Dermat. & Syph., **15**:30, 1927.
5. Wende: Jour. Cut. Dis., **2**:14, 1904.
6. Engman and Mook: Jour. Cut. Dis., **28**:275, 1910.
7. Kanoky and Sutton: J.A.M.A., **54**:1137 (April) 1910.
8. Wise and Lautman: Jour. Cut. Dis., **33**:441, 1915.
9. McLeod: Brit. Jour. Derm., **43**:420, 1931.
10. Pines: Arch. Dermat. & Syph., **40**:1016 (Dec.) 1939.
11. Wise and Sulzburger: Yearbook of Dermatology, p. 235, 1939.
12. Tobias: Arch. Dermat. & Syph., **18**:224, 1928.
13. Kittredge: Arch. Dermat. & Syph., **30**:537, 1934.
14. Beinhauer: Arch. Dermat. & Syph., **32**:469 (Sept.) 1935.
15. Tulipan: Arch. Dermat. & Syph., **37**:22, 1938.
16. Calhoun and Brown: Arch. Dermat. & Syph., **11**:183 (Feb.) 1925.

DISCUSSION (*Abstract*)

Dr. Everett S. Lain, Oklahoma City, Okla.—Dr. Hundley and Dr. Smith have explicitly described a rare disease. So far as I am able to ascertain, there are less than fifty cases reported in American literature, though Europeans have been writing about this condition and talking about it in much larger groups of cases. My own experience with this disease has been limited to four cases, and none of these was of the acquired type

such as has been presented today. They were each an hereditary or congenital type.

Engman, Sr., and Mook called our attention to this disease and presented two cases in 1905 which were published in the *Journal of Cutaneous Diseases*. They presented two additional cases in 1909, and another in 1912, a total of five cases.

Since that time Dr. Fred Wise, in 1915, reported a case which has been mentioned by the essayist. The histopathology of the case reported by Wise and Lottman differed considerably from that of Engman's cases. Engman, Sr., especially emphasized that in his cases there was an absence of normal elastic fibers which seems to have established the opinion in America that it was a congenital, hereditary, pathologic defect. This opinion still prevails, I think, among the majority of the dermatologists. I concur in that opinion.

Very few cases of the acquired type have been reported. The most recent case was reported last year by Dr. Pines in the Dermatological Society of the Bronx, where several physicians took part in the discussion, one of whom was Sparks Oppenheim, of Austria. He seemed to be quite familiar with the disease. In fact, there are more of these cases of the acquired type reported in European literature than in our own. Oppenheim was decidedly of the opinion that the so-called acquisita cases were merely of delayed development and could be classified as epidermolysis bullosa tarda. After reviewing the history of the cases this seems to be a logical conclusion.

Dr. Smith's patient showed evidence of dystrophy of the nails for twenty years, though he denied having the bullae from which we ordinarily make the clinical diagnosis. That leads me to believe, with the further record of the case as related, that this man could possibly be classified as one of the consanguine or intermarriage type. In the copy of the paper which you furnished me, Dr. Smith, you made a footnote to the effect that this patient died recently from a cardiovascular trouble. Perhaps the cardiovascular changes which came to him in later life might have been remotely related pathologically to the syndrome of epidermolysis bullosa.

The cases which I observed several years ago in two girls were of the congenital hypertrophic type that had previously been diagnosed by the late Dr. J. B. Shelmire. They were congenital; also the family history indicated that there might possibly be some blood relationship between the parents.

Another case which I have treated was that of a girl whose mother alleged the bullae did not appear until she was 14 years old. This might have been classified as the acquired type. I had occasion to observe her several times, and she had some dystrophy of the nails. She later married and it was my privilege to see her again in our state hospital after she had been delivered of a baby. I was called in consultation for the reason that her obstetrician had diagnosed herpes gestationis or impetigo. I then noted that wherever the abdominal band had been placed and wherever the slightest trauma had occurred she had bullae.

Dr. Lamb, of our clinic, diagnosed a case of the simple type four years ago, and I had occasion to see this case a few days ago. This young fellow is not yet showing any sluggish mental development nor dystrophic skin. He shows only the macules and slight pigmentation of the skin where the lesions have previously occurred.

I shall hereafter be more cautious in the taking of histories of all such benign bullous eruptions. I am also wondering if some of these cases that have been reported in the past as the acquired type might not now fall into the category of benign familial pemphigus, which has recently been well presented by Howard Hailey.

Dr. Andrew L. Glaze, Birmingham, Ala.—The problem presented by Dr. Hundley's case must be admitted as insoluble in the light of the knowledge at hand, but it is interesting to speculate about it. As Dr. Lain mentioned, the condition is considered a recessive instead of a dominant in genetics. Rare diseases like this one, as we know, require that the individual carrying the gene, or the gamete of the disease on the gene, must find the mate somewhere carrying the same one before the disease can be reproduced in the offspring.

It has been estimated that in a mixed population, subject to flow or mixture, not like mountain people or Caucasians who live in the same community, the chance is one in fifty thousand that any individual marrying in the general population will marry someone carrying a gene of the disease. Our imagination can tell us how many generations, perhaps through a hundred or two hundred or three hundred or more years, would have to pass before the average individual carrying the gamete of this disease on his gene would find a mate to carry the same one and thereby reproduce the disease in the offspring, granting, of course, that this is a case of tardy heredity.

There are known cases of recessive heredity in which the disease does occur late in life. To explain those, if the speculation had been made that the fragility or imbalance or dysplasia inherent in the particular tissue, in this case perhaps the elastic tissue, waits on changes produced by senility, advancing age, changes in the endocrine balance or what not to throw the delicate balance off so that the mechanism of the disease can be reproduced, that of course gets into the field of speculation, but it is the speculation of the expert geneticists.

Dr. Robert Brandt, Augusta, Ga.—Siemens has stated that there are two types of inheritance in epidermolysis, the dominant type and the recessive type. In the dominant type of inheritance, of course, it is necessary that one of the parents have manifest lesions of the same type. In the recessive type it is not necessary because, as Dr. Glaze has said, both genes must be united in one person to give manifestations of this type. The probability of this occurrence is much larger in the case of consanguinity of the parents. Most of the cases of dystrophic epidermolysis have been observed in such a condition. In Dr. Smith's case there was consanguinity of the parents and frequent consanguinity in the family history. Usually the number of siblings is too small to get a correct percentage, but in this case there are nine siblings, so it should occur in at least two of them, not only one.

CAR WINDOW ELBOWS*

By HOWARD B. SHORBE, M.D.
Oklahoma City, Oklahoma

Automobile transportation has brought many new and characteristic fractures. These include "bumper fractures" of the tibia and fibula; "dashboard" knees and hips; and "windshield faces." The modern trend of widening cars, plus the fixed habit of many drivers of resting the left arm on the window ledge, has now added another injury, much more mutilating and serious: "car window elbows." These are becoming increasingly common and this is not mitigated by the fact that the results, even under ideal treatment, often leave a severely disabled arm. They may be prevented by the simple means of not driving or riding with the arm resting on the car window.

A car window elbow is typically a severe compound comminuted explosive type of fracture of the lower humerus and upper radius and ulna. Injury to the great nerves, vessels and other soft parts is common. The usual case is that of a man about 30 years old, driving with his left arm resting on the window frame. As he passes a wide truck, or another car too closely, he experiences a severe stinging pain in the elbow. He is stunned to find that it is seriously mutilated, with one to several wounds, from which broken parts of bones protrude. His arm is useless. Shock comes early and may be profound.

Thirty-two consecutive cases of injury caused by riding with the elbow in a car window are reviewed in this paper. All have been treated, at least partially, by the writer. They have been seen in all stages, from the initial acute injury, immediately following the accident, to the late stage; at least eight years after the accident. Many of them were not seen until after infection with osteomyelitis had developed. Fixed deformities were already present in some. The results found in this series may well be considered an average.

The cause and frequency of this injury has been recognized, yet the literature is sparse and there has been no active campaign of prevention. Speed and Boyd[1] briefly discuss the condition in a publication concerning general treatment of fractures about the elbow. Trimble and Brantigan[2] point out the dangers and seriousness of car window injuries and cite several cases. Schrock[3] added an excellent method of treatment to certain types.

It is not practicable to give a complete epitome of each of the thirty-two cases. Therefore, they have been tabulated carefully and results of the group obtained.

Thirty-one patients were males and one was a female. The average age was 27 years. The left arm was injured in 25 patients and the right in 7. Twenty-seven patients stated they had been sideswiped by another car; 12 were injured by the overhanging edge of a wide truck. It is possible that others of the remaining 15 may have been struck by a truck, but our histories did not relate this. Two right arms were injured by striking the side of a bridge. One elbow struck a horse, another a mule, and one came too close to a corner. One man's arm was struck as he signaled to make a left turn. Of the thirty-two patients, 24 had compound fractures.

An attempt has been made to classify these fractures and dislocations so that treatment may be more definitely rationalized.

Two cases were fortunate enough to have only a slight injury to the soft tissues about the elbow. These were minor, although one patient had considerable pain and swelling for several days following the injury.

The most minor of fractures occurred in only one bone; usually the olecranon or the proximal end of the ulna. Three cases of this type were seen.

The next group is much more severe. The radius and ulna are fractured, or there may be a dislocated head of the radius with a severely comminuted ulna. Nine cases were in this class.

Fractures of the humerus alone were seen in six cases. They consist either of a fracture of the lower end, with severe comminution into the joint, which may truly pulverize the entire condylar area, or fractures of the lower third of the shaft. Occasionally a fracture of the middle third was seen.

The last type is the most severe of the group and consists of fractures of the humerus and of the forearm bones, usually extending into the elbow from each side. There were 12 cases in this class. Treatment is much more difficult and, as is to be expected, results are less desirable. Nerve involvement is common and it is not infrequent to find fractures of the metacarpals

*Read in Section on Bone and Joint Surgery, Southern Medical Association, Thirty-Fourth Annual Meeting, Louisville, Kentucky, November 12-15, 1940.

with severe lacerations of the hand, apparently due to jerking the hand from the wheel and striking it against the side of the car.

A study of the wounds of these cases and their associated fractures throws some light on their original cause. If the very tip of the elbow is struck it is likely that an olecranon fracture will result. If the elbow is far out of the window and the blow strikes well down the forearm, the second type will result with fractures of both bones of the forearm. If the arm is thrown against the rear frame of the window, there will be an associated humeral fracture. The most probable force producing a humeral fracture alone is a blow striking the flexed elbow at the base of the olecranon and exploding the lower humerus, or forcing it back against the window and fracturing it in the mid shaft.

Nerve injuries are rather frequent complications. There were six ulnar nerve paralyses, five radial and two median. This is exclusive of arms which were amputated immediately or later.

Treatment of these cases is difficult to evaluate, in that all were not treated at one clinic immediately after the injury. However, in reviewing the types of treatment it was found that seven were cared for by closed manipulation; skeletal traction was employed in ten; one case had excision of the distal end of the humerus; three patients had to have removal of the head of the radius; the entire proximal third of the ulna was excised in one case; open reduction was done in nine; and bone graft was done in six instances. Some of these forms of treatment necessarily overlapped. Several patients received skeletal traction and excision of the head of the radius, for example. Bone graft was usually done after other methods had failed. In some of the bone grafts vitallium plates were also used to assist in internal fixation.

The complications of this group are rather outstanding. One patient had diabetes and developed considerable infection. There were eleven cases that developed osteomyelitis of varying degrees of severity. There were three amputations. Two of these were for gas gangrene and one followed gangrene with an occluded brachial artery. One patient died of gas gangrene.

The final results of these 32 elbows are as follows: excellent, with a normal or nearly normal extremity, 4 cases, of which 2 had no fractures.

Good, with a useful range of motion in the

Fig. 1 A
Fracture of both bones of the forearm, dislocating the head of the radius. Before treatment.

Fig. 1 B
After skeletal traction and excision of the head of radius.

elbow, no nerve involvement and a useful hand, 5 cases.

Fair, with useful but limited elbow; some weakness of the arm and possibly some nerve involvement, 9 cases.

Poor, with slight motion to a rigid elbow, moderate to severe nerve involvement, but with a slightly useful hand, 4 cases.

Fig. 2 A

Proximal end of the ulna; dislocation of the head of the radius. Severe comminution.

Fig. 2 B

Result after excision of the proximal end of the ulna. Fair motion; good strength in flexion; and good stability.

Eight patients had an entirely useless extremity.

There was one death and one patient is still under active treatment.

It is easily seen that this type of injury is likely to result unfavorably in a high percentage of cases. The useless extremities all resulted from injury to both the radius and ulna, and the humerus, or to the lower humerus alone, in which there was severe damage to the soft parts including the nerves, as well as to the bone.

This series is not large enough to show definitely that even the severe injuries, if treated properly, would obtain more satisfactory results. We feel that with the present treatment of compound fractures with the use of sterile cleansing and the instillation of sulfanilamide, results will be better.

The patients receiving early efficient treatment were found to recover more quickly and with the least morbidity. In this connection a very careful initial examination, to ascertain the extent of nerve, blood vessel, bone and muscle injury, is absolutely essential.

The accepted treatment of a compound wound has been described many times. That which has the nearest approach to ideal consists of thorough cleansing of the wound, using large quantities of sterile water and tincture of green soap to lavage the injured tissues. This is followed by debridement with the removal of all possible contaminated tissue. As a rule, loose bone is removed. Sulfanilamide crystals are now shaken into the open wound before closure. The wounds are sutured tightly unless loss of tissue is too great for immediate closure. If so, vaselized gauze is packed into or laid over the remaining wound or cavity. It may be found practicable to apply skin grafts over some areas, but this depends entirely upon the time following the accident, the amount of dirt present, and the operator's skill. The administration of combined tetanus and gas gangrene antitoxin is routine, after testing for sensitivity to horse serum.

In the treatment of the fractures probably the most useful single method is skeletal traction. Traction in bed with wires to the lower radius and olecranon will often align some of the most severe fractures. In addition, one has free access for treatment of the compound wound and the removal of the swelling that invariably accompanies the injury is facilitated. After being certain of minimal infection and optimal posi-

tion, a cast, either long arm or shoulder spica, incorporating the Kirschner wires, may be applied. Open reduction of almost any fracture is criticized by many. In fractures about the elbow the ability of the surgeon, the question of infection and the extent of injury all must be weighed carefully. Very extensive bone injury with no infection may frequently be restored practically to normal position and alignment by a competent surgeon. Schrock[3] has recently described a most valuable technic in restoring and maintaining the severely comminuted fractures of the proximal ulna with anterior dislocation of the distal fragment of the ulna and of the head of the radius. A heavy steel nail, similar to a Steinmann nail, is inserted into the olecranon and down the realigned shaft of the ulna. Advantages of this are the relative ease in holding the fragments and the possibility of early motion. This type of open surgery may be done at the initial cleansing of a compound fracture when sulfanilamide is used.

Fig. 3 A
Severe explosion fracture of the lower humerus

Fig. 3 B
Result after excision of the fragments, and reshaping the lower end. There are good motion and stability.

Extensive comminution of the lower humerus is frequently best treated by early removal of the small fragments and reshaping the remaining condyles. This partial excision of the joint is followed, many times, by surprisingly good elbows. Instability and some weakness usually result, but motion is good. The early use of plating, when indicated, may prevent the development of nonunion or malunion. Nonunion is frequent enough and the type of fractures with occasional infection make a bone graft very difficult and often a dangerous procedure.

Divided nerves should be sutured as early as possible. Injury to a large blood vessel, particularly the brachial supersedes all other management and after ligation or suturing it is essential that it be established that circulation will be sufficient before any other work is attempted.

In conclusion, the car window elbow is the most serious and disabling of injuries peculiar

Fig. 4
Severe fracture of the lower end of the humerus and upper end of the radius and ulna, with extensive soft tissue damage and brachial artery occlusion. The results were gangrene and amputation.

to the automobile, and yet its prevention is simplicity itself: keep your elbows inside your car.

BIBLIOGRAPHY

1. Speed, J. S.; and Boyd, H. B.: Fractures About the Elbow. Amer. Jour. Surg., New Series 38, No. 3, 1937.
2. Trimble, I. Ridgeway; and Brantigan, O. C.: Crushing Injuries to the Arm Which is Protruded Through the Automobile Window Frame. Internat. Surg. Digest, 24:3-7 (July) 1937.
3. Schrock, Robt. D.: Side-Swipe Fractures at the Elbow (to be published).

DISCUSSION (*Abstract*)

Dr. Hugh Smith, Memphis, Tenn.—Car window elbows or side-swipe fracture is a term descriptive of a mechanism rather than a fracture. This mechanism is capable of producing a great variety of weird and bizarre fractures. There is no rule of thumb or routine method of treatment.

Many of these cases would ordinarily be eligible for very extensive internal fixation except for the fact that two-thirds of them are compound fractures. The problem is application of efficient internal fixation with minimal trauma and a minimal amount of metal. That is rather satirical, "extensive internal fixation," after seeing the results secured by hanging casts; I still think, however, that internal fixation in these compound comminuted fractures is a necessity.

We have used the Schrock or Rush method to great advantage when there are comminuted fractures of the ulna. This procedure is preferable, when indicated, to more extensive methods of fixation and to conservative measures, such as skeletal traction.

After the usual technic for the compound wound, a Steinmann pin is introduced through the olecranon and thence down the intramedullary canal. In the presence of extreme comminution of the ulna, particularly in fractures of the upper third, circular wire loops must augment the pin. With a fracture through the olecranon, a loop should be passed around the proximal fragment and through holes drilled through the distal fragment, as proper apposition is difficult to maintain even with a threaded pin. "Blind" insertion of the pin without exposure of the fracture site or sites of the ulna in closed fractures is impractical.

With extreme comminution of the elbow joint, we prefer assembling the parts as well as possible, even should ankylosis ensue, rather than to resort to resection and the possibility of a flail elbow. Then months, or even years later, motion may be secured by arthroplasty.

Dr. Charles F. Wood, Louisville, Ky.—The only point in this excellent presentation that has not, in my opinion, been emphasized sufficiently is the high incidence of amputations necessarily resulting from this injury. It has been my experience, and that of other men with whom I have discussed this injury, that approximately 50 per cent of the arms so injured require amputation. This is true both in private practice and in the Louisville City Hospital, where at least half a dozen cases of this injury are treated each summer. While I do not feel that amputation is justified because of the severity, extent or complexity of the fractures, it is all too often necessary because of complete obliteration of the blood supply to the hand or because of the extensive, mangling soft tissue damage. In some cases, too, traumatic amputation has occurred.

As a matter of interest, I would merely like to mention an instance where two of these injuries occurred simultaneously, one to the driver and the other to the occupant of the left rear seat of the same car. Both suffered multiple comminuted fractures of the ulna, radius and humerus in addition to complete mangling of the soft tissues of the lower arm, elbow, and forearm. This damage was so severe that amputations were necessary, both cases being seen by three surgeons.

By far the best treatment of this lesion is its prophylaxis.

Dr. Shorbe (closing).—Dr. Wood has discussed an interesting treatment which has not been in general use, or, at least, it was not when these cases were gathered, and certainly it is applicable in many cases.

Dr. Schrock's method should be considered in all possible cases. Unfortunately, we had not many in which it might have been used.

Again I stress the fact that excision of bone fragments is not recommended. My lantern slides pointed that out. In the two cases in which it was used in the entire series of thirty-two cases, it was almost a necessity. In the one there was no soft tissue covering the ulna at all, and in the other there were several reasons why it seemed to be the most reasonable method of treatment, and the final result justified excision.

The primary thing is prevention. In the event one does get a car window elbow, with the proper use of treatment of compound fractures we can reduce the morbidity to far below what has been shown in these figures. The figure of 50 per cent is rather high for amputations. That was my opinion until I looked up the thirty-two cases, and it was found that only three required amputation in the entire series.

THE PATHOGENICITY OF STRAINS OF BRUCELLA OBTAINED FROM CASES OF HODGKIN'S DISEASE*

By WILEY D. FORBUS, M.D.

and

J. U. GUNTER, M.D.

Durham, North Carolina

INTRODUCTION

In 1939, Parsons and Poston[1] reported from our laboratory a group of four cases of human brucellosis in which our gross and histologic study revealed the findings of typical Hodgkin's disease. One of these cases was studied at autopsy, and Brucella was cultivated from many tissues. Since then we have studied at autopsy four cases of unmistakable Hodgkin's disease and

*Read in Section on Pathology, Southern Medical Association, Thirty-Fourth Annual Meeting, Louisville, Kentucky, November 12-15, 1940.

*From the Department of Pathology, Duke University School of Medicine, Durham, North Carolina.

from each of these cases Brucella has been isolated.

These observations have led us to a restudy of the reactions of the human host and the experimental animal to infection with Brucella since they seemed to suggest the possibility that human brucellosis and Hodgkin's disease may be closely related pathologic processes.

The possible importance of these observations with reference to the etiology of Hodgkin's disease was recognized, although the number of cases studied was admittedly small. Emphasis has been added to the potential significance of these findings by another observation which we have made, but which we have not yet published except in preliminary form, namely, that an extraordinarily high percentage of lymph nodes exhibiting the usual diagnostic features of Hodgkin's disease may yield Brucella when properly cultured.[1 2 3] While we have had no reason to doubt the accuracy of our findings, we have nevertheless felt called upon to subject them to the most critical tests possible before proceeding with studies designed to test the suggested possible etiologic role of Brucella in the Hodgkin's disease process.

The first step toward this end was quite naturally to check the identification of the organisms which have been obtained from the Hodgkin's cases. This seemed especially important in view of the widely recognized difficulties attending the isolation of Brucella from tissues and the complex cultural and serologic reaction of these organisms, all of which together may give rise to grave error in identification of bacteria of this group. Accordingly we have carried out two procedures. The first consisted of an entirely independent restudy of the cultural and serologic characteristics of our organisms by workers who had had no previous experience with these particular bacteria, but whose experience with Brucella elsewhere than in our own laboratories was extensive.* The second consisted in a series of experiments designed to study the pathogenicity of the organisms in question for the guinea pig.

In this paper are reported the results of a series of experiments executed to determine (1) the pathogenicity of the organisms obtained from the above mentioned cases of fatal Hodgkin's disease and identified culturally and serologically as Brucella and (2) the infectivity of tissues obtained at autopsy for the experimental animal. Guinea pigs were chosen for the experiments, since their susceptibility to Brucella infection is well known and the lesions which characterize the infection have already been described.

*These studies were made principally by Grace Kerby, formerly bacteriologist of the Brucellosis Laboratory of the Clayton Foundation for Research and now working in our laboratory. Miss Kerby's work confirmed the identification of the organisms as Brucella in 4 of the 5 cases (strains designated II, III, IV and V in this paper). The organism originally isolated from the fifth case (strain I in this paper) was independently identified as Brucella, shortly after its isolation, at the National Institute of Health in Washington.

EXPERIMENTAL MATERIALS

Tissues obtained at four of the autopsies and organisms isolated at autopsy from all five cases were used for inoculation.

For orientation of the materials and the organisms used for the inoculations a brief summary of the respective autopsies follows. The detailed clinical and pathologic findings in these cases will be the subject of a subsequent communication.

Case 1.—Autopsy 2034, R. W., a white male, aged 26 years, died after an illness of about 14 months. The spleen, liver, bone marrow, lungs and all lymph node groups showed the typical gross and histologic picture of Hodgkin's disease. Brucella suis was obtained in culture from lymph node, liver, spleen and testis. This organism will be referred to in the reports of animal inoculation as Strain I.

Case 2.—Autopsy 2471, S. G., a white man, aged 38 years, died following an illness of 14 months' duration. Extensive Hodgkin's disease was found at autopsy involving the spleen, liver, diaphragm, bone marrow and all lymph nodes. Brucella melitensis was cultured from the spleen, liver, kidney, pancreas and several lymph nodes. This organism is designated Strain II.

Case 3.—Autopsy 2721, P. W., a negro male, aged 30 years, died after an illness lasting 12 months. At autopsy, Hodgkin's disease was found with specific lesions involving the spleen, bone marrow, liver, adrenals, kidneys and all groups of lymph nodes. Brucella melitensis was cultured from the spleen. This strain will be referred to as Strain III.

Case 4.—Autopsy 2728, G. B., a white lad, aged 13.5 years, died following a chronic illness of seven years' duration. Autopsy showed Hodgkin's disease involving the spleen, liver, diaphragm, pleura, adrenals and all lymph nodes. Brucella suis was obtained from the ascitic fluid and from an axillary lymph node. This strain will be referred to as Strain IV.

Case 5.—Autopsy 2780, W. M., a white male, aged 37 years, died after an illness lasting 3.5 years. At autopsy, the specific lesions of Hodgkin's disease were seen in the lymph nodes everywhere, the spleen, bones and bone marrow, lungs, trachea, pleura and retroperitoneal tissues. Brucella melitensis was cultivated from the spleen and other organs. This strain was called Strain V. An organism isolated from the blood of this patient about one month before death was also identified

as Brucella melitensis and will be referred to as Strain Va.

ANIMAL INOCULATIONS

(A) *Inoculation of guinea pigs with tissues obtained at autopsy on four cases of Hodgkin's disease (summary of data, Table I).*

Various materials from the autopsies were used. Blocks of tissue were obtained from representative organs in as aseptic a manner as possible, using a red-hot blade to sear the surface and sterile instruments to remove two or three grams of tissue. A suspension of each tissue was prepared by macerating it in a mortar with sterile sand and a few cubic centimeters of normal saline. One c. c. of tissue suspension was injected intraperitoneally into each guinea pig. Bile from two cases was also used. Inoculations were made as soon after obtaining the tissues as possible, usually within two hours.

The guinea pigs, both males and females, used in all of these experiments, weighed approximately 250 to 350 grams each. A few members of each shipment of animals were given a skin test with brucellergin, and were examined for agglutinins to all varieties of Brucella to rule out possible natural Brucella infection.

No animals were inoculated with tissues from *Case 1*.

Experiment 1.—The materials for the inoculations were obtained from *Case 2*. Twenty-nine guinea pigs were used. Five were inoculated with liver, two with a normal area of spleen, two with an area of spleen involved by Hodgkin's disease, two with pancreas, two with testis, two with rib marrow, two with bile, two with kidney, and ten with lymph nodes from several locations.

Two of the animals died a fortnight after inoculation from pulmonary infection. The remaining pigs were killed at intervals varying from 2 to 6 months. In one of the animals inoculated with pancreatic tissue and killed after 14 days, gross lesions suggestive of Brucella infection were found in one of the lymph nodes. These lesions consisted essentially of focal areas of necrotic leukocytes surrounded by mononuclear cell proliferation (macrophages), the resultant appearance being that of a chronic abscess. In another animal inoculated with axillary node tissue suspension, a focal reticulo-endothelial proliferation was observed in and about the peripheral sinuses of some of the lymph nodes. This reaction bore striking resemblance to the reticulo-endothelial reaction of both focal and diffuse character seen so constantly in the animals inoculated with the virulent strains of Brucella to be described shortly. The spleen was cultured from most of the animals of this group, but no organisms were obtained. Gram-positive cocci were demonstrated in bacterial stains of the chronic abscess-like lesion, but no organisms were seen in the other sections. Stains of the sections for tubercle bacilli were negative in all lesions observed.

It may be added that several guinea pigs were inocu-

TABLE I

INOCULATION OF GUINEA PIGS WITH SUSPENSION OF TISSUES FROM CASES OF HODGKIN'S DISEASE

CASES OF HODGKIN'S DISEASE	CULTURES OF TISSUES AT AUTOPSY	TISSUE INOCULUM	ANIMALS INOCULATED	LESIONS FOUND AT ANIMAL AUTOPSY	CULTURES AT AUTOPSY ON ANIMALS	STAINS OF ANIMAL LESIONS FOR BACTERIA ALL TYPES	DURATION OF EXPERIMENT	FATE OF ANIMALS
R W AUT 2034	BRUCELLA SUIS	0	0	0	0	0	—	—
S G. AUT 2471	BRUCELLA MELITENSIS	LIVER SPLEEN PANCREAS TESTIS RIB MARROW BILE KIDNEY LYMPH NODE	29	1 CHRONIC ABSCESS LYMPH NODE 1 R.E. HYPERPLASIA LYMPH NODE	NEGATIVE	GRAM-POSITIVE COCCI, CHRONIC ABSCESS. LYMPH NODE NEGATIVE	2 WEEKS TO 6 MONTHS	KILLED
P W AUT 2721	BRUCELLA MELITENSIS	SPLEEN KIDNEY LYMPH NODE LIVER	10	4 GRANULOMA LIVER, SPLEEN OMENTUM	NEGATIVE	ACID FAST BACILLI	5 WEEKS TO 6 MONTHS	KILLED
G B AUT 2728	BRUCELLA SUIS	SPLEEN LIVER KIDNEY LYMPH NODE BILE	10	1 FOCAL NECROSIS LIVER	NEGATIVE	NEGATIVE	2 WEEKS TO 5 MONTHS	KILLED
W M. AUT. 2780	BRUCELLA MELITENSIS	SPLEEN LIVER LYMPH NODE	5	NONE	NEGATIVE	NEGATIVE	1 TO 3 5 MONTHS	KILLED

lated with lymphoid tissue and blood from this patient during his life. When these animals were killed and examined at autopsy they failed to show any lesions.

Experiment 2.—The tissues used for inoculation were obtained from *Case 3.* Ten pigs were injected: two with spleen, two with liver, two with kidney, two with axillary lymph node, and two with mesenteric lymph node.

One of the pigs died in 6 weeks. The remainder were killed at intervals varying from 5 weeks to 6 months. Only four pigs showed lesions of any significance. One of these animals, killed 6 months after injection with axillary lymph node, had extensive lesions in the liver, spleen and omentum. The liver lesion was suggestive of brucellosis and consisted of a large area of necrosis infiltrated with neutrophils and eosinophils and enclosed in a wall formed of epithelioid cells. The lesions in the spleen and omentum, however, were unusual for brucellosis in that the areas of hyaline necrosis were small and masses of a curious tissue composed largely of cells resembling epithelioid cells were exceedingly abundant. Mitoses were occasionally seen in these. There was a marked increase in the amount of fibrous tissue and a few hyalinized fibrous scars were seen. Furthermore, there were many giant cells of the Langhans type. No growth was obtained from culture of any of the animals. Stains of sections for tubercle bacilli revealed in the lesions acid-fast organisms, whose morphology was consistent with that of the tubercle bacilli. Stains for other bacteria were negative. The second animal in this group showing significant lesions revealed a mononuclear wandering cell reaction in the omentum somewhat comparable to that of the first animal just described. In the other two infected animals lesions were found in the omentum and spleen qualitatively like those in the first animal, but quantitatively quite limited. No bacteria of any sort were demonstrated in the lesions of these animals. Nevertheless, the lesions in all four animals were considered to be of the same etiology.

Experiment 3.—Materials from *Case 4* were used to inoculate ten guinea pigs: two with spleen, two with liver, two with kidney, two with axillary lymph node, and two with bile.

Four of these animals died with a pulmonary infection about 1.5 months after inoculation. The remainder were killed at intervals varying from 2.5 weeks to 5.5 months. Only one animal showed lesions. This one was inoculated with liver and was killed 18 days later. The lesions were located in the liver and consisted of focal areas of necrosis infiltrated with neutrophils and surrounded by a wall of granulomatous tissue. Brucella was not obtained in culture from any of this group of pigs. Stains of sections showing the lesions revealed no organisms.

Experiment 4.—Five guinea pigs were inoculated with tissues from *Case 5:* two with spleen, one with liver, one with axillary node, and one with mesenteric node.

These animals were killed at intervals varying from 1 to 3.5 months after inoculation. None showed any lesions characteristic of Brucella infection and no growth was obtained from their spleens.

SUMMARY OF FINDINGS FROM DIRECT INOCULATION OF HODGKIN'S TISSUE

(1) Guinea pigs were inoculated intraperitoneally with suspensions of a variety of tissues from each of 4 cases of Hodgkin's disease, including the liver, lymph nodes and spleen, and observed for periods varying from 2 weeks to 6 months.

(2) Lesions suggestive of brucellosis on gross and microscopic examinations were observed at autopsy in animals inoculated with tissues from 3 of the 4 cases of Hodgkin's disease. Of 54 guinea pigs inoculated with Hodgkin's tissue from 4 cases only 7 animals exhibited lesions of any sort. These were distributed as follows: two from *Case 2,* four from *Case 3,* and one from *Case 4.*

(3) Animals exhibiting lesions showed no clinical evidence of disease, the lesions being discovered only after sacrifice at predetermined times and in some instances only by extended histologic examination.

(4) Brucella was not recovered from inoculated animals either with or without lesions.

(5) The lesions in one of the two positive animals inoculated with tissues from *Case 2* contained gram-positive cocci. The lesions in the other animal were not sufficiently characteristic to be interpreted as the specific result of Brucella infection and no bacteria of any sort could be demonstrated in them.

The lesions in one of the four positive animals inoculated with tissues from *Case 3* contained acid-fast bacilli, presumably tubercle bacilli. The lesions in the other three animals were comparable histologically to those in the first animal and were considered to be of the same etiology, although neither acid-fast nor other organisms were demonstrated in them.

The lesions in the only positive animal inoculated with tissue from *Case 4* were not sufficiently typical of Brucella infection to warrant their being so considered. Neither acid-fast nor other forms of bacteria could be found in sections appropriately stained.

(6) From the foregoing summary of our results of inoculation of guinea pigs with Hodgkin's tissue we conclude that we have neither reproduced the pathologic anatomical lesions of Hodgkin's disease nor have we produced guinea pig brucellosis. While the experiments therefore do not show the presence of Brucella in Hodgkin's tissues, they do not at the same time exclude its presence, since the single theoretical

factor of a low concentration of organisms in the tissues may account for the negative results. The failure of our experiments to show the presence of Brucella in presumably infected tissues is not out of harmony with the experience of others who have used for inoculation the tissues of known Brucella infected animals. Nevertheless, serial infections have been accomplished in this manner.

(7) Our experience with the guinea pig as a test animal for determining the presence of Brucella in tissues indicate that observations based upon superficial examination of the sacrificed animal are probably worthless. The most critical study of all lesions found is essential if error is to be avoided.

(B) *Inoculation of guinea pigs with Brucella obtained by cultures made from tissues at autopsy on five cases of Hodgkin's disease (summary of data, Table II).*

Inoculation with Brucella Strain I.—This organism was kept in the frozen state for about a year before being used for inoculation. Experiments with it were designed to study the local response and the lymph node reaction to Brucella infection, the general body reaction, the effect of repeated inoculation, the effect of massive doses, and the effect of serial mouse inoculations on the virulence of the organism. Several experiments were done before it was concluded that the strain possessed little capacity to infect guinea pigs. These experiments are recorded in brief as follows.

Experiment 5.—The purpose was to study the local response and the lymph node reaction to infection with Strain I. Thirty-five guinea pigs were inoculated subcutaneously on one side of the abdominal wall with doses of a half-billion organisms of this strain in 0.5 c. c. normal saline. Each was given a control injection of saline on the opposite side. The animals were killed in groups of 5 pigs each at intervals of 3/4, 1, 2, 3, 4, 5 and 6 days after inoculation. In each pig the site of injection of the organisms and control areas were studied histologically, as were also the regional lymph nodes, the spleen and in some instances other organs. A few animals showed local tissue reaction resulting most probably from trauma. No growth was obtained from cultures of the spleens.

Experiment 6.—This experiment was designed to study the general body reaction to infection with Strain I. Eighteen guinea pigs were injected intraperitoneally with one billion organisms, and were killed at intervals varying from 1 to 13 weeks. No lesions which might be attributed to Brucella infection were found either grossly or microscopically. Spleen cultures were negative. No agglutination developed, and the opsonocytophagic indices remained normal.

Experiment 7.—Four guinea pigs were inoculated intraperitoneally with one billion organisms of Strain I, and in 10 weeks were reinjected with an equal dose. Two were killed in two weeks and the remainder in six weeks after reinoculation and no lesions were found.

TABLE II

PATHOGENICITY FOR THE GUINEA PIG

OF STRAINS OF BRUCELLA OBTAINED FROM CASES OF HODGKIN'S DISEASE

STRAIN OF BRUCELLA	INTRAPERITONEAL INOCULUM IN BILLIONS	ANIMALS INOCULATED	ANIMALS INFECTED	RECOVERY OF ORGANISMS FROM INFECTED ANIMALS	LESIONS PRODUCED	STAINS OF LESIONS FOR BACTERIA ALL TYPES	DURATION OF EXPERIMENT	FATE OF ANIMAL
I B SUIS AUT 2034	2-256 FROZEN STOCK	89	13	HEART BLOOD AND PERITONEUM 13	PERITONEUM	MANY GRAM-NEGATIVE COCCO-BACILLI	24 HRS	DIED
II B MELITENSIS AUT 2471	2 FROZEN STOCK	16	0	0	0	NEGATIVE	7 DAYS TO 8 WEEKS	SACRIFICED
III B MELITENSIS AUT 2721	2 CURRENT LAB CULTURE	16	11	SPLEEN 6	LIVER LYMPH NODES OMENTUM EPIDIDYMIS SPLEEN	NEGATIVE	7 DAYS TO 5 MONTHS	SACRIFICED
IV B SUIS AUT 2728	2 CURRENT LAB CULTURE	16	11	SPLEEN 2	LIVER EPIDIDYMIS PERITONEUM LYMPH NODES	NEGATIVE	7 DAYS TO 5 MONTHS	SACRIFICED
V B MELITENSIS AUT 2780	2 CURRENT LAB CULTURE	16	9	SPLEEN 5	EPIDIDYMIS LIVER LYMPH NODES SPLEEN	NEGATIVE	14 DAYS TO 3 MONTHS	SACRIFICED
Va B MELITENSIS AUT 2780 ANTE-MORTEM BLOOD CULTURE	2 CURRENT LAB CULTURE	16	7	SPLEEN 1	EPIDIDYMIS LIVER LYMPH NODES	NEGATIVE	10 DAYS TO 4 MONTHS	SACRIFICED

Experiment 8.—In view of the negative results obtained from the preceding experiments, it was thought advisable to try large doses to determine the size of dose which would produce infection. Meanwhile, an attempt was made to increase the virulence of Strain I by serial mouse inoculations. After passage through a series of mice the strain became so virulent that a small dose would kill a mouse in less than 24 hours. With the presumably highly virulent organisms, sixteen guinea pigs were inoculated. Two were inoculated intraperitoneally with two billion organisms, two with four billion, and so on, with doses increasing by geometrical progression so that the last group received 256 billion organisms.

Thirteen of the animals died within 24 hours after inoculation, and most of these died in less than 12 hours. The findings in all were essentially the same. The peritoneal vessels were engorged and the peritoneum appeared acutely inflamed with patches of gray exudate on the omentum. Microscopically (*Fig. 12*) the omentum was densely infiltrated with an exudate consisting chiefly of macrophages and neutrophilic leukocytes. Gram-negative coccobacilli in exceedingly large numbers were seen on the peritoneal surfaces and invading the omentum. A variety of stains was employed to demonstrate the organisms. The Giemsa method was found to stain them most sharply. The peritoneal exudate and the heart blood of five animals were cultured and the organism was recovered from both locations in each pig.

The three animals which survived received relatively small doses of two, two and four billion organisms. They were killed in 10 weeks and showed no lesions and no growth was obtained from their spleens.

Experiment 9.—This experiment was begun before the last three animals in the preceding experiment were killed. The assumption from experiment 8 was that the optimum dose was 2 billion organisms. Consequently, sixteen guinea pigs were inoculated, each receiving 2 billion organisms of Strain I, rejuvenated by

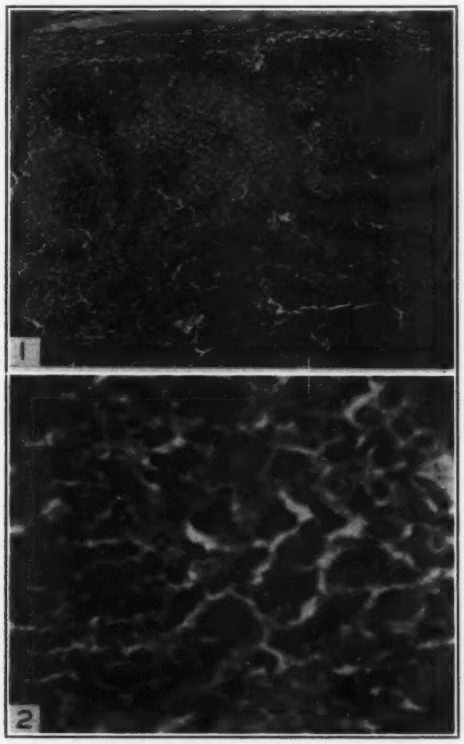


Fig. 1. Experimental brucellosis, guinea pig 97. Lesion in lymph node 4 weeks following intraperitoneal inoculation of Hodgkin's autopsy Strain V, B. melitensis. Extensive diffuse reticulo-endothelial reaction with epithelial transformation of cells and giant cell formation producing destruction of normal lymph node architecture and replacement of lymphoid tissue.

Fig. 2. Same as *Fig. 1.* High power view of an area of reticulo-endothelial reaction with epithelioid transformation of cells and multinucleated giant cell formation.

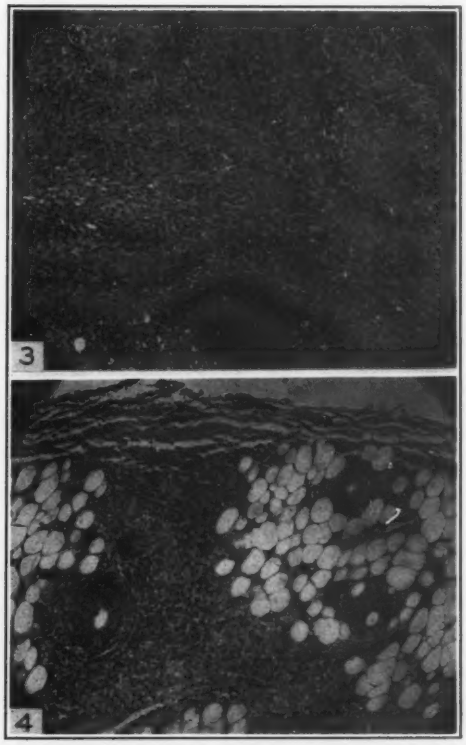


Fig. 3. Experimental brucellosis, guinea pig 22. Lesion in omentum 7 days after intraperitoneal inoculation of Hodgkin's autopsy Strain III, B. melitensis. Epithelioid reaction about an area of necrosis and leukocytic reaction. Same section as in *Fig. 4.*

Fig. 4. Same as *Fig. 3.* Reticulo-endothelial reaction with beginning epithelioid transformation of cells in the omentum with special localization about blood vessels and lymphatics. Same section as in *Fig. 3.*

serial mouse inoculations. Two pigs were killed at weekly intervals, the last group of two being killed in 8 weeks. No lesions were found in any of the animals except a chronic nonspecific inflammatory reaction in the omentum in a few instances. The organism was not recovered in culture.

Inoculation with Brucella Strain II. Experiment 10.—Sixteen pigs were injected intraperitoneally with 2 billion organisms of this strain which, like Strain I, had been frozen for several months. Serial mouse inoculations were not done. The animals were killed in pairs at weekly intervals. No lesions were found in any of them and the organisms were not recovered in culture.

Inoculation with Brucella Strain III. Experiment 11.—Sixteen pigs were injected intraperitoneally with 2 billion organisms of this strain which had not been frozen. The data on these pigs are recorded in *Table 2*. The Brucella lesions referred to in the table are described in detail in a subsequent section. Blood from two of these animals tested at the end of 3 months for agglutinins showed none.

Inoculation with Brucella Strain IV. Experiment 12.—Sixteen pigs were inoculated intraperitoneally with 2 billion organisms of this strain which had not been frozen. The data on these pigs are recorded in *Table 2*. Blood from two of these pigs tested at the end of 3 months for agglutinins showed none.

Inoculation with Brucella Strain V. Experiment 13.—Sixteen guinea pigs were inoculated intraperitoneally with 2 billion organisms of this strain which had not been frozen. The data on these pigs are recorded in *Table 2*. Blood from two of these animals tested at the end of 6 weeks for agglutinins showed none.

Inoculation with Brucella Strain Va.—Sixteen guinea pigs were inoculated intraperitoneally with 2 billion organisms of this strain which had not been frozen. The data on these pigs are recorded in *Table 2*. Blood from two of these animals tested at the end of 2 months for agglutinins showed none.

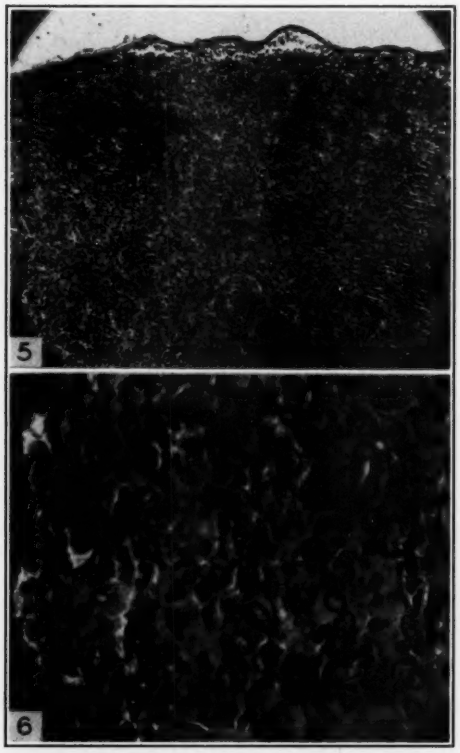


Fig. 5. Experimental brucellosis, guinea pig 63. Lesion in lymph node 3 weeks after intraperitoneal inoculation of B. melitensis strain Va (same as Hodgkin's autopsy Strain V, but obtained by blood culture one month before death of patient). Diffuse reticulo-endothelial reaction with epithelioid transformation of cells with destruction of normal architecture and virtually complete replacement of lymphoid tissue throughout the node. Compare with *Fig. 1*.

Fig. 6. Same as *Fig. 5*. High power view of reticulo-endothelial reaction and epithelioid transformation.

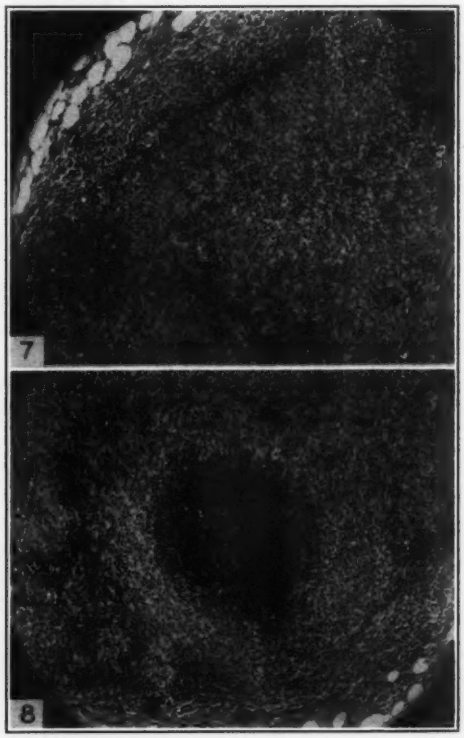


Fig. 7. Experimental brucellosis, guinea pig 48. Lesion in lymph node 4 weeks after intraperitoneal inoculation with Hodgkin's autopsy Strain IV, B. suis. Diffuse reticulo-endothelial reaction and epithelioid transformation producing destruction of normal architecture and replacement of lymphoid tissue throughout the node. Compare with *Fig. 1* and *Fig. 5*.

Fig. 8. Same as *Fig. 7*. Focal necrosis and leukocytic infiltration, abscess-like lesion, in same lymph node as shown in *Fig. 7*. Compare with *Figs. 3, 9* and *10*.

SUMMARY OF FINDINGS FROM INOCULATION OF GUINEA PIGS WITH STRAINS OF BRUCELLA CULTURED FROM CASES OF HODGKIN'S DISEASE

(1) Six strains of Brucella were obtained by cultural methods from 5 cases of Hodgkin's disease. Five of these strains were derived from tissues at autopsy and one from the blood during life.

(2) Organisms obtained from autopsies on 4 cases of Hodgkin's disease and diagnosed bacteriologically and serologically as Brucella were confirmed as such as shown by their ability to produce in guinea pigs lesions typical of Brucella infection in these animals. A fifth organism obtained from blood culture during the life of one of the autopsied cases produced typical lesions of brucellosis in guinea pigs, which lesions were identical with those produced by the Brucella strain obtained at autopsy.

(3) Brucella obtained at autopsy from one case of Hodgkin's disease produced no lesions in guinea pigs.

(4) One of the four strains which proved infectious for guinea pigs differed from the other three in its capacity to infect to a remarkable degree, huge doses of organisms being required for positive inoculation in contrast to the relatively small doses of the other organisms required for infection.

(5) Tests of the blood from two of the inoculated animals in each of the experimental groups revealed no specific agglutinins for Brucella between six and eight weeks following inoculation, at which time specific lesions may be presumed to have existed.

(6) The Hodgkin's strains of Brucella which proved infectious for guinea pigs were found to differ from the usual strains found in lower animals in two respects. In the first place the rate of experimental infection is lower as indicated by the fact that only 51 of 153 animals (33 per cent) inoculated with virulent organisms became infected. In the second place, although the lesions produced were typical of guinea pig brucellosis the distribution of the lesions was somewhat atypical.

DISCUSSION

The pathologic changes found in guinea pigs infected with Brucella abortus have been described by Fabyan[4] and others. According to Huddleson,[5] the lesions in guinea pigs are essentially the same with all strains of Brucella.

According to our experience, the typical Brucella lesion which we have used as a standard in the morphologic diagnosis of guinea pig brucellosis begins within about one week after inoculation (*Figs. 3, 4, 5, 8, 9, 10* and *12*). The first tissue changes consist of a focal accumulation of large mononuclear wandering cells which appear to originate through the proliferation of cells of the reticulo-endothelial system. These cells which are macrophages proliferate rapidly as indicated by the frequency of mitotic figures observed and thus give rise to a microscopic nodule (*Fig. 10*), the cells of which are quite uniform in type, before secondary changes occur

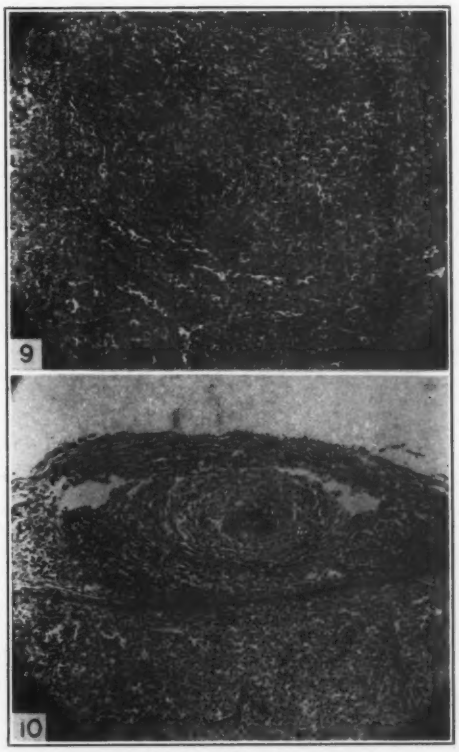


Fig. 9. Experimental brucellosis, guinea pig 105. Lesion in spleen 3 months after intraperitoneal inoculation of Hodgkin's autopsy Strain V, B. melitensis. One of several epithelioid focal reactions with beginning necrosis and leukocyte infiltration at the margin of a lymphoid follicle.

Fig. 10. Experimental brucellosis, guinea pig 30. First stages of development of typical Brucella reaction in the splenic periosteum observed 12 weeks after intraperitoneal inoculation of Hodgkin's autopsy Strain III, B. melitensis. Focal reticulo-endothelial reaction forming an epithelioid nodule followed by necrosis of the centrally situated cell and inwandering of neutrophilic and eosinophilic polymorphonuclear leukocytes. Compare with *Figs. 9, 11, 3* and *8*.

in the lesion. Before the macrophagic or reticulo-endothelial nodule develops beyond microscopic size secondary changes occur. These consist of a transformation of the mononuclear cells into elements of epithelioid type, the latter forms sometimes containing several nuclei. Such multinucleated giant cells (*Figs. 2* and *6*) occasionally develop further with the formation of giant cells resembling the usual Langhans giant cell. Giant cells of Langhans type are, however, not common and are not in any sense a characteristic feature of the brucellosis lesion. Concurrent with the epithelioid transformation of the mononuclear cells necrosis of the centrally situated cells occurs (*Figs. 8, 9* and *10*) a development which is quickly followed by the inwandering of neutrophilic leukocytes. These cells soon overwhelm the mononuclear cells in the central zone, and, presumably under the influence of the organisms or their products, they, too, suffer death and disintegration. While this is in progress eosinophilic leukocytes slowly wander into the peripheral zone of the lesion and may be seen scattered among the epithelioid cells, whence they wander further to become concentrated at the margin of the necrotic central area. The fully developed typical lesion thus takes on the rather general gross appearance of a chronic abscess (*Fig. 8*) and consequently the term "abscess" has been used quite generally in describing the lesions of brucellosis.

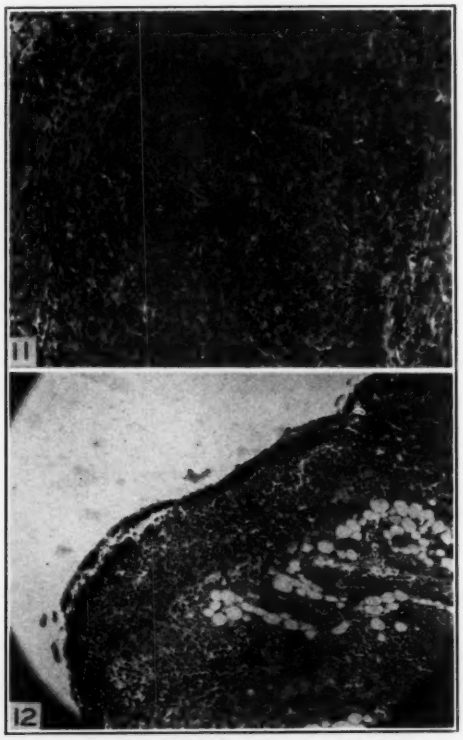


Fig. 11. Experimental brucellosis, guinea pig 41. Lesion in epididymis 7 days following intraperitoneal inoculation of Hodgkin's autopsy Strain IV, B. suis. Reticulo-endothelial reaction with beginning central necrosis and polymorphonuclear infiltration accompanied by peripheral epithelioid transformation.

Fig. 12. Experimental brucellosis, guinea pig G-VI-2. Reaction in omentum 12 hours after intraperitoneal inoculation of Hodgkin's autopsy Strain I, B. suis. Predominant reticulo-endothelial reaction accompanied by neutrophilic polymorphonuclear leukocytes. Great number of gram-negative coccobacilli free on surface and within cytoplasm of macrophages and leukocytes.

That the lesion is in no sense an abscess is at once evident to any one who has followed the course of development. The lesion is on the contrary a reticulo-endothelial reaction with epithelioid transformation and terminal necrosis, quite comparable in pathologic principle to the granulomatous reaction exemplified by tuberculosis, Hodgkin's disease and a variety of fungus infections.

As in these diseases the brucellosis lesion is characterized by many variations, though such variations do not appear to be frequent. Two variants have impressed us in this series of experiments. One of these is seen particularly in the lymph nodes and consists of an almost complete and uniform replacement of the lymphoid tissue by the reticulo-endothelial reaction which appears to take place through the coalescence of many foci of proliferation (*Figs. 1, 2, 5, 6, 7* and *8*). The lymph node may thus lose its normal architecture except in restricted areas, just as it does, for example, in Hodgkin's disease. Focal necroses usually occur before the node is completely transformed by the cell proliferation and an epithelioid transformation of the reacting cells is already recognizable before the proliferative response is complete (*Fig. 8*). The other variant of the brucellosis lesion which may have special significance is the rapid epithelioid transformation of the macrophages resulting in a characteristic granulomatous lesion with multiple necrotic areas reminding one of the lesions of Hodgkin's disease. It is worth emphasizing that such lesions do not contain genuine tubercles nor is the composition of the lesion such as to suggest tuberculosis other than as a bare possibility. Nevertheless, it is obviously quite possible to confuse the lesion with certain atypical tuberculous reactions. Because of this, in our interpretation of the guinea pig

lesion we have carefully excluded any confusion with tuberculosis by diligent studies of the lesions for tubercle bacilli (*Table 2*), even though the inoculated Brucella organisms were recovered from the animal by splenic cultures.

The brucellosis lesions in our animals have all appeared to be progressing. Nothing has been seen indicating healing except fibrotic change in the granulomatous lesions. Some of our animals were infected for five months so it would appear that in the guinea pig brucellosis may be a highly chronic disease, the end stages of which have not as yet been satisfactorily studied.

In no instance have we been able to demonstrate Brucella in the tissues by bacterial stains of the lesions with the exception of the earliest (12 hour) lesions in the peritoneum. This is true not only of the experimental lesions, but also of the Hodgkin's tissues. We have, however, been able to exclude the presence of other organisms, including the tubercle bacillus, by both strains of the tissues and cultures.

In the group of experiments concerned with the direct inoculation of tissues from four of the autopsies, a total of 54 guinea pigs was used. None of these showed typical Brucella lesions. In the group of experiments concerned with the inoculation of cultures obtained from the five autopsies, no specific lesions were produced by one of the strains (Strain II). With the other five strains obtained from four cases, 153 guinea pigs were inoculated and 51, or about 33 per cent of these, showed lesions which could be attributed to Brucella. It follows that cultures are more reliable for obtaining the organisms from Hodgkin's tissues than are animal inoculations with these tissues.

The inoculations made with Strain I, the results of which are included in the above figures, deserve special mention. Eighty-nine animals were inoculated by a variety of routes and only 13 infections (14 per cent) were produced, all the result of intraperitoneal inoculation. In none of these 13 were lesions found outside the peritoneal cavity, although exceedingly large numbers of organisms were introduced, a striking contrast to the results of inoculation of other strains after which lesions were found in the liver, spleen and lymph nodes in addition to the peritoneum, and in approximately 60 per cent of the inoculated animals. We have no satisfactory explanation of the relatively insignificant infectivity of Strain I and the total lack of ability of Strain II to infect the guinea pig. Both organisms had been preserved in the frozen state for several months before use for inoculation, Strain I much longer than Strain II. Whether freezing alone may influence the pathogenicity of Brucella we do not know. We are at present using frozen stock for our current studies in dogs and pigs, but it is as yet too soon to know whether our animals have been successfully infected. Our experiments as a whole indicate that the strains of Brucella obtained from these cases of Hodgkin's disease were not as virulent as the bovine strains used by Fabyan, who had no difficulty in producing the experimental disease. Whether this low virulence is to be related to long residence in the body in association with the Hodgkin's process, an attractive point of view, remains to be shown.

Our failure to demonstrate specific agglutinins in the Brucella infected animals deserves some comment, though an explanation of the absence of agglutinins is not at hand. In the cases of Hodgkin's disease from which our Brucella strains were isolated Brucella agglutinins have usually been absent. However, in other cases of Hodgkin's disease still being followed in our clinic and from which we have isolated Brucella by culture of the excised lymph nodes, specific agglutinins for Brucella have been demonstrated, though they do not appear to be constantly present.

In the infected animals the epididymis (*Fig. 11*) was involved in about 90 per cent of the male pigs used. Fabyan found changes in 40 per cent (including the testicular lesions proper). The lymph nodes (*Figs. 1, 2, 5, 6, 7* and *8*) showed lesions in 15, or about 30 per cent, as contrasted with 95 per cent lymph node involvement obtained by Fabyan. The omentum, mesentery and other peritoneal structures (*Figs. 3, 4, 10* and *12*) showed infection in 25 pigs, or about 50 per cent. The spleen (*Fig. 9*) was specifically involved in only two animals, or about 4 per cent, as contrasted with splenic involvement in 95 per cent of Fabyan's animals.* Lesions occurred in the seminal vesicles in two of our pigs, and in the uterus and kidney in one instance each. In some animals the lymph nodes, spleen and lungs (interstitial mononuclear cell pneumonia) showed changes suggestive of Brucella infection, but these were not considered

*This extraordinary discrepancy is doubtless accounted for on the basis of the criteria used. Only spleens showing characteristic granulomatous lesions confirmed by microscopic study and containing no demonstrable bacteria including tubercle bacilli have been considered positive in our work. Fabyan's criteria appear to have been less exacting.

sufficiently specific to justify their being attributed to Brucella. Bone and joint involvement, a common feature of Fabyan's animals, occurred in none of ours.

CONCLUSION

(1) At five consecutive autopsies on cases of typical Hodgkin's disease, Brucella has been cultured in each case from a variety of tissues. In three of the cases the isolation of these organisms was accomplished independently by more than one worker. The identification of these organisms was subsequently confirmed by independent workers who had had no part in their isolation.

(2) Suspension of tissues from each of 4 of the cases were inoculated intraperitoneally into a total of 54 guinea pigs. In no animal were typical lesions of guinea pig brucellosis produced. This observation is in harmony with the experience of others with animal inoculation of tissues from cases of Hodgkin's disease, but obviously does not exclude the presence of pathogenic organisms in these tissues.

(3) Pure cultures of each of the Brucella strains isolated from the 5 cases of Hodgkin's disease were inoculated intraperitoneally into a total of 169 guinea pigs. Four of the 5 strains proved to be capable of producing a mild form of guinea pig brucellosis. The fifth strain was not pathogenic for the guinea pig.

(4) These and our previous studies show that the tissues in an extraordinarily high percentage of our cases of Hodgkin's disease harbor Brucella of the suis or melitensis variety and that these organisms are fully capable of producing typical experimental brucellosis in the guinea pig, although they appear to be distinctly less virulent than similar organisms isolated from natural infections in the lower animal.

(5) These experiments were not designed and do not pretend to prove that the Hodgkin's lesions in our cases were produced by the organisms found in the tissues. That they suggest an etiologic relationship is obvious.

We wish to acknowledge our indebtedness to Dr. Bowman Wise for autopsy cultures, some of the animal inoculations, and the agglutination tests and opsonocytophagic indices; to Miss Mary Poston for autopsy cultures, and for aid in inoculation of some of the animals; to Mr. W. A. Mickle for the serial mouse inoculations; and to Dr. D. W. Goddard for aid in performing autopsies on some of the guinea pigs.

REFERENCES

1. Parsons, Philip B.; and Poston, Mary A.: Sou. Med. Jour., **32**:7-13 (Jan.) 1939.
2. Poston, Mary A.; and Parsons, Philip B.: Jour. Infect. Dis., **66**:86-90 (Jan.-Feb.) 1940.
3. Parsons, Poston, and Wise: Pathology of Human Brucelliasis. Amer. Jour. Path., **15**:634-635 (Sept.) 1939.
4. Fabyan, Marshal: A Contribution to the Pathogenesis of *B. abortus*. Bang II. Jour. Med. Res., **26**:441-487, 1912.
5. Huddleson, I. Forest: Brucella Infections in Animals and Man, p. 23. Oxford University Press, 1934.

DISCUSSION (*Abstract*)

Dr. George T. Caldwell, Dallas, Tex.—Those of us who attended the meeting at Oklahoma City, where the first paper dealing with this subject by Parsons and Poston was presented, were greatly impressed by the significance of the implications underlying the findings presented at that time. The paper which has been presented here this afternoon seems to add very definitely to certain phases, at least, of the interpretations made at that time.

All of us who knew of earlier attempts to cultivate organisms from lymph nodes in Hodgkin's disease were naturally somewhat skeptical about the frequency of the incidence of the Brucella organisms in Hodgkin's lesions. It seems to me, therefore, that this report today makes it plainly evident that an organism which has the cultural characteristics of Brucella of the different types has been isolated from at least five fatal cases of Hodgkin's disease; and, secondly, that these organisms which have been isolated have produced lesions in guinea pigs that are characteristic of experimental brucellosis.

Of course, the relationship of these organisms to the underlying disease diagnosed as Hodgkin's disease still must be considered with some concern. Whether they may be incidental invaders in tissues which are already damaged by disease must, first of all, be taken into consideration. That I think can be satisfactorily settled in the near future, when other laboratories have cultivated organisms from lymph nodes or other tissues from patients with Hodgkin's disease more successfully than they are able to do at the present time.

Other laboratories have had great difficulty up to the present time in confirming these bacteriologic findings. That may well be the fault of the bacteriologic technic in those laboratories, and I doubt that fair tests have been made along this line.

Then, secondly, as all of you know, a number of years ago, in 1934, Fitchett and Weidman pointed out that in a negro boy of 18 who had histologic Hodgkin's disease an organism of the Cryptococcus type was found in the lesions. In studying the literature they found there were two other cases in which a systemic Cryptococcus infection was associated with lesions which were histologically like those of Hodgkin's disease.

My attention was directed to these findings by a case which was reported by Dr. May Owen, of Fort Worth, in 1940. This was a patient in whom the diagnosis of Hodgkin's disease had been made by a number of observers, and I am afraid that included me, since I had seen sections of the lesions and thought they were typical of Hodgkin's disease. In the later course of this disease process, Cryptococci could be seen in sections from other lymph nodes and from other parts of the body at autopsy, which made the diagnosis of systemic cryptococcosis, although the histologic changes

were similar, if not identical to those which we usually diagnose as Hodgkin's disease.

So I am wondering if one agent, or several different agents, may be responsible for the series of changes which eventuate in what we call Hodgkin's disease.

I should feel more certain about the multiplicity of causative agents if it were not for the fact that practically all of the cases which we call Hodgkin's disease histologically follow practically the same fatal course, and that makes it seem rather unlikely that there are multiple agents responsible for the peculiar type of proliferation which we recognize as Hodgkin's disease.

Dr. M. Pinson Neal, Columbia, Mo.—Three questions of much potential importance occur to me. If the authors are not prepared to reveal answers to them, they may be content in withholding them for later presentations.

First, have animal inoculations been attempted by other than the intraperitoneal route? It is known that certain tissues are peculiarly sensitive or susceptible to some organisms, while others are highly resistant, especially by artificial inoculation.

Second, have inoculations been repeated at five, seven or ten-day intervals, taking advantage of the supposed breakdown of resistance or establishment of sensitivity?

Third, have animals other than guinea pigs been used?

Dr. Elizabeth Gambrell, Emory University, Ga.—I think the authors are to be congratulated on the excellent paper presented, because we know there is no more involved question today than that of brucellosis and of its relation to Hodgkin's disease.

We have had few cases of Hodgkin's disease in Emory University Hospital, and we have tested them by all the known tests for brucellosis; that is, agglutination test, skin test, the phagocyte reaction, and cultures, and they have been negative to all of these tests. Two autopsies were done confirming the diagnosis of Hodgkin's disease. In no case have we obtained a positive culture.

I should like to ask the authors what method of culture other than animal inoculation can be used. I am here seeking knowledge, because I have been very unsuccessful myself, and I feel that it is possibly the fault of the bacteriologist that we do not obtain more positive cultures.

There are certain other points I would like to bring out in regard to the paper, if I may. First, the organisms isolated in these cases were most unusual, in that they are Brucella suis and Brucella melitensis. The melitensis, for example, are considered rather rare in this country. I should like to ask, was Brucella suis ever isolated from the blood of the patient? Usually, in infections with Brucella suis, we have very little trouble in obtaining growth of the organism from patients with brucellosis, and I was wondering whether or not it was possible to get it by blood culture from the patients with Hodgkin's.

It seems to me that this paper emphasizes the involved epidemiology of the disease. Here we have five cases of Hodgkin's, showing cultures of Brucella suis and Brucella melitensis, and not of Brucella abortus, which is most commonly found and possibly the organism to which we are most constantly exposed. I wonder whether that is due to the low virulence of this organism.

We are all watching with a great deal of interest the work that is being carried on at Durham.

Dr. Roy R. Kracke, Emory University, Ga.—As Dr. Gambrell has already pointed out, at Emory University we have attempted to isolate Brucella from five cases of Hodgkin's disease, including material from two cases at autopsy and three from biopsy.

In a written communication Dr. McGath, of the Mayo Clinic, says that he has been unable to isolate the organisms from several cases of Hodgkin's disease.

Although it may not be pertinent to this paper, I should like to know what we are doing that is wrong, and in what way our bacteriologic technic may be deficient. I believe that we use acceptable technics for cultivation of Brucella. If there is some special technic employed for the recovery of these bacteria, I should like very much to know about it.

Dr. Oscar B. Hunter, Washington, D. C.—We have had a number of cases of Hodgkin's disease since I first heard the report in Oklahoma City of its possible relationship to brucellosis. A case which we have had under observation for about two years is a young man who has been traveling all over the United States, from whom we removed a gland, cut it in half, sent one-half to Dr. Forbus and ran the other half through ourselves. Unfortunately, we were unable to get a positive culture in either instance.

This young man has been to the University of Michigan and a number of other clinics as far West as Kansas City, and he has had about six glands removed.

We have been keeping track of him, but in so far as I know no one has yet recovered an organism. We feel that it is a case of Hodgkin's disease and this diagnosis has been concurred in by the majority of the members of the Washington Society of Pathologists.

If the authors have any further suggestions concerning the technic of examination we should welcome them, with a view of the possibility of making a further examination of this patient at a later date.

Dr. Forbus (closing).—The questions that have arisen in your minds, I assure you, have also arisen in ours. We have been working, therefore, with the same degree of suspicion and criticism of the whole matter that you have expressed in your various comments.

It was not our intention to discuss at this time the question of the possible specific etiologic relationship between Brucella and Hodgkin's disease, which has been suggested both by our previous communications and by the paper which we have just presented. We feel that an attempt to discuss this problem at the present time woud probably be premature since the extent of observations pertinent to the question is as yet far too limited to exclude from such a discussion a great deal of pure speculation. I do feel, however, that from the data already at hand it is possible for us to be assured of one very helpful and, I think, incontestable fact. A careful consideration of the available observations leaves no doubt that the basic reaction and responses of tissues to infection by Brucella are fundamentally the same as those which occur in the Hodgkin's process. I think it further possible to say that there is nothing which characterizes either

the organism Brucella or the responses which it provokes which would eliminate that organism from consideration as a possible etiologic agent in Hodgkin's disease. While these facts seem to be clear we are certainly in no position to say at the present time that the organism with which we are concerned here is the cause of Hodgkin's disease. I think that I can assure you that even if the relationship between Brucella and Hodgkin's disease as brought out in the cases which we have presented can be shown in the future to be a constant occurrence, it will still be an extremely difficult accomplishment to establish beyond question the suggested specific etiologic relationship. As I see the matter, the significance of this relationship can be established only by future work of a most critical nature and in volume sufficient for sound statistical analysis, which work must be planned to test the constancy of occurrence of Brucella in Hodgkin's tissue. I am not too hopeful of being able to reproduce classical Hodgkin's disease in the experimental animal. I suspect that we shall have exhausted the possibilities of this approach to the solution of the problem when we have shown that one or a variety of experimental animals respond to infection by Brucella through the development of a granulomatous reaction which is in principal and in essential detail similar to, if not identical with, the reactions which characterize the Hodgkin's process. The reactions of the tissues of the guinea pig which we have shown you today represent what we feel justified in believing to be a first step in the accomplishment of that end.

Dr. Caldwell has raised the question of the possibility that there is more than one agent capable of producing Hodgkin's disease. He recalled the case of Fitchett, a case studied in great detail by Weidman, of Philadelphia, and reported as a combination of Cryptococcus infection and Hodgkin's disease. Through the splendid cooperation of Dr. Weidman, we have had opportunity to study at length not only all of the materials from that case but also a large group of materials from experimental animals which Dr. Weidman had used in studying reactions produced by the specific Cryptococcus strain obtained from the Fitchett case. Study of these materials left us with the feeling that the Fitchett case is probably an instance of a combination of Hodgkin's disease and Cryptococcus infection. It is surely well known to all of us that Cryptococcus does not in its usual form produce a lesion which is readily confused with that of Hodgkin's disease. This is certainly true as far as our own experience goes.

Furthermore, the experimental disease in animals which was produced by Weidman with the organism from the Fitchett case bears little resemblance to the Hodgkin's process. Through the courtesy of Dr. Tracy Mallory we have had opportunity to study another case which has been described as a combination of Cryptococcus infection and Hodgkin's disease. This case was presented at one of Dr. Mallory's Clinical Pathological Conferences, the notes of which were published in the *New England Journal of Medicine*. My own study of the sections from the Mallory case left me with the feeling that the resemblance of the reaction to the Cryptococcus to that of the Hodgkin's process was only an apparent one, that the case was in reality simply one of cryptococcosis, and that it did not represent a genuine instance of a combination of an infection with this organism and Hodgkin's disease. In Dr. Mallory's report of his case he mentions having seen other cases of this sort. Although I have had the fullest cooperation in the matter, I have not as yet been able to locate the other cases which he mentioned.

Throughout our own investigations of the relationship between Brucella and Hodgkin's disease, we have been aware not only of the reports of combinations of cryptococcosis and Hodgkin's disease in the same individual, but also of other combinations. The majority of our bacteriologic studies on the Hodgkin's materials have, therefore, been carried out with all of the necessary precautions for determining the presence of the various pathogenic fungi. Since none of our cultural studies have demonstrated the presence of Cryptococcus or other fungi in the Hodgkin's tissues from our cases, we have felt justified in eliminating these organisms from consideration as possible etiologic agents in the disease under consideration, and have felt content to regard cases such as those of Fitchett and Weidman and Mallory either as simple coincidental occurrences of Cryptococcus infection and Hodgkin's disease or as atypical instances of pure Cryptococcus infection. In so doing we are fully aware of the possibility that our own observations of combinations of Brucella infection and Hodgkin's disease may likewise prove to be simple coincidences.

Although we recognize the fact that the morphologic response of the tissues to a variety of infectious agents may be basically that which characterizes the response in Hodgkin's disease, illustrations of which I need not discuss, we have chosen to adopt the view that Hodgkin's disease is both an etiologic and a pathologic entity, and that the disease represents a response of the body to a single etiologic agent. This view I do not believe is out of harmony with that entertained by Dr. Caldwell. This point of view is at least a practical one in so far as the etiology of this disease is concerned. To think of Hodgkin's disease as a response to infection by a variety of organisms or agents makes for almost unsurmountable difficulty, and I fear may be responsible for a fairly widespread attitude which has caused some to feel that it is rather hopeless to attempt to solve the etiologic problem. We have adopted the point of view that the agent responsible for Hodgkin's disease can and will be eventually uncovered. Whether or not Brucella is that agent is a matter for investigation, as we see it in view of our experiences, and not a matter at the present time for argument.

Answering Dr. Neal's question concerning modes of inoculation of our animals, I may say that in the experiment reported today all of our inoculations were done intraperitoneally. Experiments in progress in our laboratories at this time in which the dog and the hog are being used, are being carried out by intravenous as well as intraperitoneal inoculations, these inoculations being repeated at weekly intervals. In the experiments reported today, the infections produced, with one exception, were the result of single inoculations. In the experiments reported today we have used only the guinea pig. We chose this animal because of its known susceptibility to infection with Brucella and because the reactions of the tissues in this animal are better known than those in other species. Having had little experience with the experimental disease before undertaking this work, we felt it wise to use an animal which, according to general experience, would react to the organisms in question. The result of our experiments with these animals seem to have justified their selection, since with a less susceptible animal it seems not unlikely that we

might have had extraordinary difficulty in producing infection because of the low virulence of the organisms derived from the Hodgkin's cases.

I do not feel that I can comment in any helpful way upon the negative results obtained in culturing Hodgkin's lymph nodes just described by Dr. Gambrell. The technic used in our own cultural studies will be found in the papers of Parsons and Poston and Poston and Parsons, especially the latter. Utilization of these methods has not in our own hands produced 100 per cent positive results. It would be unreasonable to expect that they should. That the methods are effective as published is indicated by our further experiences since the publication of the original observations by Parsons and Poston. Since that time we have increased the number of cases of Hodgkin's disease studied during life and subsequently at autopsy to the sum total of eight. From this series we have succeeded in obtaining Brucella at the autopsy table from six of the eight cases. It is further worthy of note that in all except two of the cases the organisms have been recovered by more than one person, sometimes as many as three, each working independently of the other. We hope very much that Dr. Gambrell will continue her studies, since as we have already stated we feel that perhaps the greatest progress in development of the problem will come through bacteriologic studies of Hodgkin's tissues by different workers and, of course, under the most critical conditions. In all of these bacteriologic studies, however, it must be remembered that repeated observations are necessary on the same case before one is fully justified in reporting a negative finding. This has been our experience with the study of biopsies, especially, and even at the autopsy where several workers have been involved, in some instances some of the workers have failed in the isolation of the organisms, while others have succeeded, although all have used the same materials.

Dr. Gambrell's experiences with the agglutination reactions and in her studies of the opsonophagocytic index in the Hodgkin's cases are quite in harmony with our own. In all of our Hodgkin's cases which have come to autopsy we have failed to find positive agglutination reactions. The opsonophagocytic index has been so variable in that group of cases that we have not been able to determine its significance. In a limited number of the Hodgkin's cases which we are following at the present time, the agglutination reaction has been positive in significant titer and the opsonophagocytic index has been sufficiently high and persistently so to justify attributing some significance to it. It is worthy of special emphasis that even in those cases where the agglutination reactions have been positive there have been periods when this reaction was totally absent. It follows, therefore, that only repeated observations of the agglutination reaction and the opsonophagocytic index can be regarded as reliable in the Hodgkin's cases.

Dr. Gambrell has asked about the culture of Brucella suis from the blood. We have succeeded repeatedly in culturing this organism from the blood in different cases of Hodgkin's disease and also in the same case. In the course of the experiments which we have reported today, blood cultures were not made. In experiments in progress in the laboratory now we are repeatedly recovering Brucella suis from the blood.

Dr. Kracke has mentioned the experiences of Dr. McGath at the Mayo Clinic in culturing Hodgkin's lymph nodes as told to Dr. Kracke by this observer. We await with much interest the complete report of Dr. McGath's studies. Any comment upon his negative results to date would, of course, be premature. Any one who has worked with Brucella is quite familiar with the fact that its cultivation and especially its isolation from tissues are difficult procedures and require experience. Nevertheless, I can see no reason why a careful worker with this experience should not accomplish what we have been able to do repeatedly if, of course, the organisms are actually present.

In Dr. Hunter's discussion the question has arisen as to whether infected materials could be shipped by mail or otherwise without interfering with the isolation of the organisms. We have had so little experience along these lines that no satisfactory opinion can be expressed. During the last six months we have received from the pathologic laboratory of the Federal Bureau of Animal Industry in Denver several shipments of presumably infected material. From one of these shipments, the spleen of a hog, we succeeded in isolating Brucella suis. The material was shipped packed in borax, which seemed to preserve it satisfactorily. I see no reason why this method should not be useful in the shipment of human materials.

NEURAL MYATROPHY AND VITAMIN E*

By W. DE GUTIÉRREZ-MAHONEY, M.D.
Nashville, Tennessee

The study of muscular atrophy flourished, as did so many other matters, in the French neurological school during the greater part of the last century. This is well evident by the eponyms which we meet in the field of clinical neuromuscular disease. The name of Duchenne (de Boulogne) was outstanding, but the man who was more responsible than anyone else for the study of neuromuscular disease at that time was Cruveilhier, a pupil of Dupuytren. Although the names of Aran[1] and Duchenne[2] have been linked with muscular wasting of the upper extremities, the observations were made under the guidance and encouragement of Cruveilhier, whose clinical description of a lady he observed in 1832, who had progressive muscular atrophy, could not be bettered.[3] He examined the nervous system and that of a second patient with the same trouble who had died in 1848, and reported that no neuropathologic changes were seen in either case. On the basis of these two observations he had interested Aran and Duchenne in subsequent

---

*Read in Section on Medicine, Southern Medical Association, Thirty-Fourth Annual Meeting, Louisville, Kentucky, November 12-15, 1940.

*From the Department of Medicine and the Laboratory for Neuropathology, Vanderbilt University School of Medicine, Nashville, Tennessee.

studies of muscular atrophy, and because of Cruveilhier's postmortem observations, they ascribed the condition to disease inherent in the muscle, entirely independent of the nervous system. However, in 1850, Cruveilhier had his third patient with the same disorder, and at postmortem in 1853 he observed that the anterior roots of the spinal cord were very greatly atrophied, although the posterior roots were normal in size. He did not see anything wrong with the spinal cord itself, although he felt that the seat of the trouble would be in the anterior horn cells. It is, of course, not at all remarkable that Cruveilhier was not able to demonstrate this lesion because his pathologic studies were made entirely with the naked eye, since he did not use the microscope. In 1861, Luys[5] recorded atrophy of the anterior horn cells in the spinal cord of a man who had atrophy of the hand and forearm. Whether or not this patient had progressive muscular atrophy is impossible to tell from the meager clinical notes, but the cellular change in this clinical condition was noted in the same year by Lockhart Clarke, who then began a series of several important communications on the histologic study of the nervous system in association with muscular atrophy. In 1867, with Hughlings Jackson,[6] he reported a case of muscular wasting in which there was atrophy of the cells of the anterior horn, of the posterior vesicular column (column of Clarke), and of the oblongata at the base of the fourth ventricle. There was also disintegration of the lateral tracts and some softening of the posterior tracts. This was the first record of the pathology of "amyotrophic lateral sclerosis" which was verified by Hayem and Vulpian[7] and Charcot and Joffroy[8] two years later. Subsequently, in 1873, Lockhart Clarke[9] reported, with an excellent clinical description, another case of progressive muscular atrophy with histologic changes in the spinal cord and brain stem, but it is important because in it were first described degeneration in the ganglion cells of the cerebral cortex which finally gave us the full pathologic picture of progressive muscular atrophy, and an explanation for the variations in the syndromes which occur clinically. This paper thus climaxed the studies on this type of neural myatrophy and closed the book for more than half a century until the first clues regarding etiology and treatment were read in the chapter which Evans[10] and his pupils began to write more than twenty years ago.

In order better to understand the ground upon which we stand, it might be well to present a simple subdivision of the different types of muscular atrophy. On the whole, they can best be divided into those which are and those which are not due to disease of the nervous system.

The muscular atrophies, with which even the most careful study has never demonstrated any lesions in the nervous system, include that large group of dystrophies (also called myopathies) which were classified for us by the heroic efforts of Erb, Leyden, Dejerine, and Gowers. They are familial disorders which have been grouped by these individuals into categories, depending on the age of their onset as well as the parts of the body first affected. There are no hard and fast rules about the muscular atrophy as regards distribution or clinical course, and there is considerable overlap from one category to another. They bear the names of these men and others, names with which you and I have struggled, and needlessly, for there are many times more variations of the dystrophies than there are types already named. Indeed, there are as many types as there are families in which they occur, and the names they should bear are those of the families rather than those of the men who first recognized them. Another one of these inherent muscular atrophies is myotonia atrophica (also called dystrophia myotonia), and not infrequently myatrophy is seen with myasthenia gravis and with thyrotoxicosis.

On the other hand, the muscular atrophies which are dependent upon disease of the nervous system are: acute anterior poliomyelitis; syphilitic muscular atrophy, with or without spasticity; neuritis due to many causes (vitamin B deficiency, chemical intoxications as lead, arsenic and thallium); trauma; metabolic disorders; and the Charcot-Marie-Tooth type of peroneal myatrophy; progressive muscular atrophy (including the many synonyms and subdivisions such as wasting palsy, amyotrophic lateral sclerosis, chronic poliomyelitis, bulbar palsy, pseudo bulbar palsy, motor neurone disease); and infantile cerebral palsy.

Of these several types of neural myatrophy, we are today concerned with those which have from their first recognition been called progressive muscular atrophy, and which have been given different names, depending upon the distribution of the wasting and whether or not spasticity was present with it. Thus one might have bulbar palsy if the lower motor neurones of the brain stem were affected, or pseudo bulbar palsy if the upper motor neurones to the bulbar nuclei were diseased, or a combination of these two possibilities; or atrophy of the muscles of the

limbs because of disease of the lower motor neurones of the spinal cord (Aran-Duchenne type), or amyotrophic lateral sclerosis if spasticity were added to this because of involvement of the lateral tracts (upper motor neurone), or combinations of all these. They are one and the same disorder, affecting mainly the motor neurones ("motor neurone disease"), and our understanding of it is due to the exhaustive pathological studies of Lockhart Clarke (1861-1873), who showed that all levels of the nervous system were affected from the cells of the cortex to the fibers of the terminal nerves.

The next chapter was opened in 1922 by Evans,[10] who noted that a certain element was necessary in the diet of rats in order to carry them through a normal gestation. He felt justified in announcing the existence of a new member of the vitamin class to which the designation X, conditionally, and later E was given. Thus vitamin E came to be known as the antisterility or fertility vitamin. Later, in 1927-28, Evans and Burr[11] [12] further observed in their rats that the suckling young of mothers deprived of vitamin E developed weakness of the hind limbs a day or two before weaning (twenty-first day), at first flaccid, later spastic, the appearance of which could be prevented by the inclusion of vitamin E containing foods in the mother's diet not later than the fifteenth day of lactation, or by administering wheat germ oil to the young nursing from mothers deprived of vitamin E. These observations were verified by Morelle,[13] Mason,[14] Olcott and Mattill,[15] and others. Later paralysis was seen by Blumberg[16] and Ringsted[17] in rats which were kept on E-deficient diets only after weaning.

In the meantime, Goettsch[18] and Pappenheimer had begun a series of analogous experiments with guinea pigs and rabbits, and there resulted what they called "nutritional muscular dystrophy;"[19] so also with ducklings. Working with day-old chicks[20] they found that three weeks after being deprived of vitamin E there developed tremors, retraction of the head, muscular weakness and somnolence, with pathologic changes in the cerebellum mainly, less so in the cerebrum and the brain stem. Within the last year muscular atrophy has been seen in vitamin E-deficient dogs by Anderson, Elvehjem, and Gonce.[21]

The pathologic study of animals with E deficient myatrophy has in this country been concerned mainly with the state of the muscles, since Pappenheimer[22] reported that there were no lesions in the nervous systems of the guinea pigs and rabbits which he and Goettsch had been studying. Olcott[23] reaffirmed this stand as regards the rat. Nevertheless, there had been reports to the contrary from abroad, for Lipshutz[24] and Einarson and Ringsted[25] have seen extensive damage to the nervous system of rats.

This was the general state of these matters when in June, 1938, the experimental and clinical observations of this report were begun.

The experimental work was as follows: rats were used and pregnant females were given a diet deficient in vitamin E but containing enough of it so that resorption of the fetuses did not take place. The mothers were then kept on an E deficient diet and the young born of these mothers, with access to no supply of vitamin E other than that supplied in the E deficient mother's milk, developed a flaccid weakness in the hind limbs at the age of about eighteen days, shortly before the period of weaning at the age of twenty-one days. If they were maintained on an E-deficient diet thereafter, many of them died, but if vitamin E was added to the diet they recovered from the weakness and continued to live in a healthy state. A certain number did live and were carried through to the late stage of the condition so that our histologic observations are concerned mainly with two groups, those which were sacrificed at the age of about three weeks, and those which were carried for longer than a year.

The entire nervous system was examined by the following methods: Nissl, for a study of the cellular elements; Herxheimer, Kulschitzky, Marchi, Spielmeyer and 1 per cent osmic acid for studying the myelin sheaths; Gros-Bielschowsky and Ramon y Cajal for axis cylinders.

In general, the changes were similar for the baby and adult rats. The nerve cells generally showed very severe changes. These were characterized by a hyperchromatic appearance of the cytoplasm with complete loss of the Nissl pattern. This homogeneous overstaining was so intense as to obliterate the nucleus and nucleolus. The cell processes were also heavily stained and for considerably long distances, frequently having the appearance of corkscrews. The cell bodies did not appear ballooned out, but were generally thinner and longer than normal. The margins of these hyperchromic cells were very sharply outlined, and there were no phagocytic cells about them. The cells frequently took on most bizarre patterns often characterized by their being elongated and thinned. A second type of

cell change was characterized by a diminution in the stainable contents. These cells appeared to be in a process of disintegration. They stained faintly, contained vacuoles, and they had also lost the Nissl pattern. These were frequently in the process of being phagocytized, occasionally to the point of being merely ghosts. In all probability they represented a late stage in the disorder which began with the previously mentioned type. In no instance did there appear to be any similarity to the retrograde reaction of Nissl, nor to the usually accepted chronic cell change. These changes were seen throughout the spinal cord in the anterior horn cells, likewise in the posterior horn cells, and in all the grey matter. The dorsal root ganglia contained a few cells which were ballooned and in which the Nissl substance was pushed to the periphery, leaving the central area very pale; the nucleus was pushed to one end of the cell. This was the only type of cell which was in a state at all resembling Nissl's retrograde reaction. These cell changes were likewise to be found in the nuclei of the oblongata such as the hypoglossal, also in the pons in the pontine nuclei, in the Purkinje cells of the cerebellum, and in the large and small cells of the brain.

Examinations with the stains for myelin sheaths all showed changes in the sciatic nerves characterized by swelling, fragmentation, ball formation, and disappearance of myelin; likewise in the nerve endings within muscle and skin. Both anterior and posterior roots were altered in the cauda equina. The long conducting pathways in the spinal cord and brain were also affected. Changes were to be seen mainly in the anterior and lateral tracts in the spinal cord which in the rat represent the spino-cerebellar and the vestibulo-spinal connections; also the posterior tracts and, to a less extent, the cortico-spinal pathways. In the brain the corona radiata and the median forebrain bundle showed changes.

The silver stains for axis cylinders demonstrated alterations in the nerves, spinal cord, cerebellum, and brain.

The glial reaction was quite marked in all areas involved.

Although the hind limbs became weak and atrophic before the fore limbs, changes were to be seen in the cells of the upper as well as of the lower spinal cord segments. On the whole, it would seem that the cellular change preceded the alterations in the nerve pathways, and as a result the muscular atrophy supervened.

Because of these changes, both clinical and histological, which followed deficiency of vitamin E in the diet of rats, changes which could be prevented if vitamin E were added to these same diets, it was felt, in spite of some dissimilarity between the clinical and pathologic pictures of these rats and of patients suffering with progressive muscular atrophy, that the administration of vitamin E to these patients might be beneficial. Because of this our first patient was treated in 1938 with "germol-E," a concentrate of defatted wheat germ oil, thereby supplying vitamin E in the natural form. During these two years we have seen and treated nine patients with the type of neural myatrophy which, it seemed from our experimental and clinical studies, would come under the E deficiency class. These nine patients might be grouped into those who improved and those who did not improve after the administration of "germol-E." Three patients showed no improvement; they all had the advanced stage of the disease and were suffering from bulbar palsies as well as peripheral wasting. The other six improved. Three of those had wasting with weakness of the hand muscles. One had wasting about the neck and shoulder girdle and the other two had very little wasting, but marked spasticity. Two of the patients with wasting of the hand muscles and one with spasticity of all limbs discontinued taking the vitamin concentrate after having noted improvement, and they fell back into their previous disability. They resumed taking the material and improvement recurred. One of these fell from grace a second time, and his condition became worse, but improved once more when he took the wheat germ oil concentrate.

With the improvement of the specific complaint of localized weakness there was a marked change in the general strength and vigor of these patients, about which they spoke spontaneously. In two patients there was filling in of the previously wasted hand muscles. One man continued to have fasciculation of his muscles, though to a diminished degree, while he improved during a two-year period of observation from his being unable to walk without a stick to his being able to run well and to return to work.

Improvement usually took place within a fortnight to a month of the administration of vitamin E, which was given to all in its natural form in capsules.* The usual dose given was about 25

*Supplied by Ayerst, McKenna & Harrison, Ltd., as "germol-E," a concentrate of defatted wheat germ oil.

mg. of alpha tocopherol daily. In one patient half this amount was found inadequate when the dose had been reduced from the 25 mg., the previously administered amount.

Because of the limited amount of vitamin E concentrate at our disposal our observations at first were restricted to such patients as we felt suffered because of a deficiency of the vitamin. That large group of muscular dystrophies was thereby ruled out since, in the first place, they are familial disorders which from analysis would not be deficiency diseases. Furthermore, from an understanding of the pathology of the dystrophies in which the nervous system is absolutely intact, it did not seem reasonable that the experimental muscular atrophy which depended upon disease of the nervous system would be even remotely related to the dystrophies in man in which there is no disease of the nervous system.

But after our observations had gone on for some time we were granted a larger allowance of the vitamin concentrate and made observations upon many of the other conditions in which muscles have atrophied; and in no instance has improvement been noted in them following administration of the same material which did improve the condition in the other patients. Thus the control observations included the muscular dystrophies, myasthenia gravis, and thyrotoxic myatrophy. Muscular atrophies which we knew were due to disease of the nervous system such as syphilitic amyotrophic lateral sclerosis and Charcot-Marie-Tooth peroneal muscular atrophy and a nonatrophic form of neurologic disease, paralysis agitans, were given the material. As mentioned before, none of these showed improvement of any kind following administration of vitamin E concentrate. One of the patients with muscular dystrophy was also given vitamin B along with vitamin E, but without improvement.

It is thus our feeling that there are some neural myatrophies due to a deficiency of vitamin E which can be corrected if identified early, and by supplying vitamin E before the condition has progressed to the stage where too many of the nerve cells have been damaged beyond their being saved.

One aspect of vitamin E deficiency in relation to the nervous system, which clinically has not yet lent itself to investigation, is the possibility that infantile cerebral palsy results from E deficiency in the mother before birth and during lactation. This might be analogous to the condition in the baby rats of our experiments.

Many causes have been given for the occurrence of infantile cerebral palsy such as trauma during a difficult labor, hemorrhage, deficient oxygen, and intra-uterine intoxication. In tracing down the cause of the trouble, frequently one is unable to attribute it to any of these suggested possibilities, and it is not unreasonable to assume that the palsy is due to a deficiency of vitamin E.

It would be very difficult to demonstrate this conclusively, for therapy would have to be instituted in the mother some time before birth. It would require the administration of vitamin E to a long and carefully observed series of pregnant women, and a control series lacking supplementary vitamin E, with subsequent calculation of the incidence of infantile cerebral palsy in the offspring of each group.

One might also administer vitamin E to new born children as soon as infantile cerebral palsy is recognized, with the hope of preventing further disability and possibly of correcting the condition itself.

REFERENCES

1. Aran, F.-A.: Recherches sur une maladie non encore decrite du systeme musculaire (atrophie musculaire progressive). Arch. gen. de med., s. 4, **24**:5-35, 172-214, 1850.
2. Duchenne (de Boulogne): De la valeur de l'electrisation localisee comme traitement de l'atrophie musculaire progressive. Bull. gen. de therap., **44**:295-304, 407-412, 438-447, 1853.
3. Cruveilhier: Sur la paralysie musculaire progressive atrophique. Arch. gen. de med., s. 5, **1**:561-603, 1853.
4. Cruveilhier: Sur la paralysie musculaire atrophique. Arch. gen. de med., s. 5, **7**:1-20, 1856.
5. Luys, Jules: Atrophie musculaire progressive; lesions histologiques de la substance grise de la moelle epiniere. Compt. rend. Soc. de biol., s. 3, **2**:80-81, 1861.
6. Clarke, J. Lockhart; and Jackson, J. Hughlings: On a Case of Muscular Atrophy, with Disease of the Spinal Cord and Medulla Oblongata. Tr. Med.-Chir., **50**:489-497, 1867.
7. Hayem, G.: Note sur un cas d'atrophie musculaire progressive avec lesions de la moelle. Arch. de physiol., **2**:263-278, 391-406, 1869.
8. Charcot, J.-M.; and Joffroy, A.: Deux cas d'atrophie musculaire progressive avec lesions de la substance grise et des faisceaux anterolateraux de la moelle epiniere. Arch. de physiol., **2**:354-367, 629-649, 744-760, 1869.
9. Clarke, J. Lockhart: Progressive Muscular Atrophy Accompanied by Muscular Rigidity and Contraction of Joints. Examination of the Brain and Spinal Cord. Tr. Med.-Chir., **56**:103-112, 1873.
10. Evans, Herbert M.; and Bishop, K. Scott: On the Existence of a Hitherto Unrecognized Dietary Factor Essential for Reproduction. Science, **56**:650-651, 1922.
11. Evans, Herbert McLean; and Burr, George O.: The Antisterility Vitamine Fat Soluble E. Memoirs of the University of California, **8**:1-176, 1927.
12. Evans, Herbert M.; and Burr, George O.: Development of Paralysis in the Suckling Young of Mothers Deprived of Vitamin E. Jour. Biol. Chem., **76**:273-297, 1928.
13. Morelle, Jean: Influence de la privation de la vitamine E chez le rat au cours de la lactation. Compt. rend. Soc. de biol., **108**:804-805, 1932.
14. Mason, Karl E.: Differences in Testis Injury and Repair After Vitamin A-Deficiency, Vitamin E-Deficiency and Inanition. Amer. Jour. Anat., **52**:153-239, 1933.
15. Olcott, H. S.; and Mattill, H. A.: Vitamin E. 1. Some Chemical and Physiological Properties. Jour. Biol. Chem., **104**:423-435, 1934.

16. Blumberg, Harold: A Growth Deficiency Disease, Curable by Wheat Germ Oil. Jour. Biol. Chem., **108**:227-238, 1935.
17. Ringsted, Axel: A Preliminary Note on the Appearance of Paresis in Adult Rats Suffering from Chronic Avitaminosis E. Biochem. Jour., **29**:788-795, 1935.
18. Goettsch, Marianne: The Dietary Production of Dystrophy of the Voluntary Muscles. Proc. Soc. Exper. Biol. & Med., **27**:564-567, 1930.
19. Goettsch, Marianne; and Pappenheimer, Alwin M.: Nutritional Muscular Dystrophy in the Guinea Pig and Rabbit. Jour. Exper. Med., **54**:145-165, 1931.
20. Pappenheimer, Alwin M.; and Goettsch, Marianne: A Cerebellar Disorder in Chicks, Apparently of Nutritional Origin. Jour. Exper. Med., **53**:11-26, 1931.
21. Anderson, H. D.; Elvehjem, C. A.; and Gonce, J. E., Jr.: Vitamin E Deficiency in Dogs. Proc. Soc. Exper. Biol. & Med., **42**:750-755, 1939.
22. Pappenheimer, Alwin M.: Pathological Changes in the Skeletal Muscles Produced by Dietary Means. Proc. Soc. Exper. Biol. & Med., **27**:567-568, 1930.
23. Olcott, H. S.: The Paralysis in the Young of Vitamin E Deficient Female Rats. Jour. Nutrition, **15**:221-227, 1938.
24. Lipshutz, Daniel: Les voies atteintes chez les jeunes rats manquant de vitamine E. Rev. neurol., **65**:221-233, 1936.
25. Einarson, Larus; and Ringsted, Axel: Effect of Chronic Vitamin E Deficiency on the Nervous System and the Skeletal Musculature in Adult Rats. A Neurotropic Factor in Wheat Germ Oil. 163 pp. London: Oxford University Press, 1938.

DISCUSSION (*Abstract*)

Dr. Seale Harris, Birmingham, Ala.—I have had a good deal of experience with vitamin E in human beings. Some twenty years ago, a woman patient about 35 years of age complained of weakness and many nervous symptoms. She was undernourished and I placed her on a diet of turnip greens and other green vegetables, meat, and a building-up diet generally. She improved in strength and in weight, and in the course of a year she came back and told me that she was pregnant. I had not known anything about the fact that she was sterile up to that time, but as the result of that experience she advised one of her neighbors who had been married for a number of years and had no children to come to me. She too was undernourished, asthenic, with some muscular weakness and so I put her on that same diet of turnip greens and spinach, peas and greens, meat and other foods containing vitamin E. In the course of a few months she also became pregnant.

Last week I saw a woman, aged 40, who complained of indigestion and vomiting. Upon examination I found that she was about four months' pregnant. She had been to me a year previously when she was underweight, undernourished and asthenic. I had put her on a diet abundant in vegetables and meat and other foods containing vitamin E, and she had become pregnant. Possibly in all these cases there was neural myatrophy, due to a deficiency of vitamin E.

It seems probable that it will be found that vitamin E is made up of two factors, deficiency of one of which causes neural myatrophy and deficiency of the other sterility.

In such cases there may be multiple vitamin deficiencies. It is a rare thing that there is a single vitamin deficiency in any individual. Vitamins should be prescribed in foods. That is the place to obtain them. The concentrates and synthetic vitamins are helpful temporarily, but the best source of all the vitamins should be the foods, and in prescribing a diet rich in vitamin E, one will prevent a great many cases of neural myatrophy.

Dr. W. B. Bean, Cincinnati, O.—I should like to ask Dr. Mahoney if any effort was made to analyze or appraise the diets of these individuals to show whether or not there had been a deficiency in vitamin E.

Dr. de Gutierrez-Mahoney (closing).—There were no very studious efforts made to determine this.

THE USE OF LIVER EXTRACT IN LUPUS ERYTHEMATOSUS*

A PRELIMINARY REPORT

By HOWARD KING, M.D.

and

C. M. HAMILTON, M.D.

Nashville, Tennessee

So much has been written about lupus erythematosus that a complete review of the subject is unnecessary. The etiology is not fully understood, but it is generally believed to be an allergic cutaneous reaction from a toxemia and there is abundant evidence to support the theory that the toxic agent is a bacteremia which may result from a tuberculous, a streptococcic, or possibly a staphylococcic focus. From this point of view, much thought has been devoted in recent years to improvement in therapy. The results of treatment of lupus erythematosus prior to the introduction of gold therapy in 1927 were quite unsatisfactory. Various procedures such as the use of quinine internally and the local application of iodine, acetic acid, carbon dioxide snow, x-rays, radium, and other agents were in vogue. None of these seemed to be of any particular value. Rest, nourishing food and general care probably accounted for whatever improvement was obtained.

Lupus erythematosus is conveniently classified in three types with certain variations: (1) discoid, (2) disseminate, and (3) fulminating. This report deals with experience in the treatment of only the disseminate type.

The first real step in therapy was made when gold sodium thiosulphate in the proper dosage was found to be reasonably safe and effective. Enthusiastic reports came from various sections of the world with the universal adoption of this new remedy, but the enthusiasm was soon dampened by discouraging rumors of serious reactions and an occasional fatality. Very little trouble

*Read in Section on Dermatology and Syphilology, Southern Medical Association, Thirty-Fourth Annual Meeting, Louisville, Kentucky, November 12-15, 1940.

was encountered with the discoid variety of the disease, but many reactions and a few fatalities had been found to occur, in particular with the disseminate type. This was especially true in the more acute and widely disseminate forms associated with leukopenia. Engman[1] was among the first to make this observation which was later more fully elucidated by Weiss, Lane and Bagby.[2] It is now well known that many of this particular type not only have a leukopenia, but are quite photosensitive[3] (Hecht and Perrin).

Within the last four years many experiments have been made with sulfanilamide by Ingels,[4] Abramowitz,[5] Belote,[6] Anderson,[7] Lindsay[8] and others worthy of mention. Some of the results have been quite promising, but others have been disappointing. The beneficial results, in a few instances, have been of short duration. Dramatic improvements were sometimes quickly followed by relapses. Sulfhemoglobinemia, leukopenia and agranulocytosis were some of the unfavorable complications. Observations of the results obtained in the treatment of the after-effects of sulfanilamide therapy with liver extract stimulated interest in this type of therapy and led to this report. Response in the first case was so prompt and impressive that it was at once determined to experiment with other cases. It should be emphasized that this is only a preliminary report and definite conclusions cannot be drawn at this early date from a small group of cases. However, the results have been so gratifying, thus far, that it is hoped that others may be stimulated to make further and possibly more complete investigations.

This work was started about fourteen months ago, but the report embraces only observations made during the first twelve months. Excluding doubtful cases, the disseminate were selected and it was felt that the wider the dissemination the more appropriate was the remedy. The diagnoses were made clinically from the distribution and well known characteristics of the lesions. Fortunately, five of the cases included in this group were presented at a meeting of the Southeastern Dermatological Association and the diagnoses were unanimously accepted. Eight cases were treated, of which six were females and two were males. The ages varied from 24 to 65 years and the white blood counts from 2,100 to 8,500. Only two of them had normal blood counts. All the patients presented lesions on the face, the neck, the ears, and the shoulders. The women had additional lesions on the V-area of the chest. All the cases had lesions on the dorsa of the hands, the wrists, and the forearms, and four of them had similar lesions on the legs. Lesions on the trunk, the hips, and the thighs were present in two cases.

The method of treatment has been largely the same as that used in pernicious anemia, since its adoption came about more or less accidentally while treating a patient with a rather severe leukopenia with 2,600 white blood cells and a hemoglobin determination of 70 per cent. This condition has apparently resulted from the administration of three doses of gold sodium thiosulphate, of ten milligrams each, intravenously. With the onset of the blood condition there was an acute exacerbation and a wide dissemination of the skin lesions. After the use of 2 c. c. of liver extract containing 5 injectable U. S. P. units per c. c., for a period of two weeks, there was striking improvement, and at the end of four months the patient was completely free of lesions and had approximately a normal blood picture. This patient had also been afflicted for several years with a fairly advanced multiple arthritis, but was ambulatory. The skin lesions have been clear and she has had practically a normal blood picture for ten months. As soon as the pronounced improvement was observed in this patient, treatment was started on four other similar cases in patients who had leukopenia and a rather low hemoglobin percentage. Two had received sulfanilamide and had shown temporary improvement, but upon development of leukopenia and a drop in hemoglobin, liver extract was substituted for sulfanilamide. Three responded completely within three months and have remained clear from eight to ten months. The fourth case showed only moderate improvement and probably deserves special comment. About half of the lesions disappeared, but the rest of the lesions are still present.

This patient was an unmarried woman, 42 years of age, presenting a few old atrophied, scar-like lesions on the nose and cheeks of two years' duration. Four weeks previously a new crop of acute, typical lesions appeared on the neck, the backs of the hands, the forearms, and the legs. The white blood count was 3,900 and the general health was poor. She was regarded as having an old discoid type with a definite acute dissemination. The acute lesions disappeared with the administration of liver extract, but the old lesions were not altered.

It is felt that two significant observations were made in this case. The discoid type does not seem to improve under this form of therapy, but acute lesions, occurring in a patient with old

discoid involvement, apparently respond like an independent acute process. This was the only case with old discoid lesions in which this method of treatment was tried.

The sixth case was a woman, 65 years of age, who had had recurring attacks of discoid lesions for a period of fourteen years and had been treated with gold therapy the previous year. She developed rather severe dermatitis and nephritis which caused her to be in a critical condition for several weeks. During this interval, the lesions disappeared, but recurred in a disseminate form the following spring and summer. She lived on a farm and was naturally exposed to the sun considerably. She was advised to have liver extract administered by her family physician, but this procedure was terminated at the end of two months. Although considerable improvement was obtained, there was not a complete resolution, which has been attributed to inadequate treatment.

The youngest patient in this series was a man 24 years of age in whom the condition had existed for two months. After receiving liver extract and cod liver oil for three months he was completely free of the eruption at the end of two months and has not had a recurrence. The other man, 52 years of age, in whom this condition had been present for two months, was given four doses of gold sodium thiosulphate. He developed a mild dermatitis and this treatment was replaced by liver extract. At the end of four months he had completely recovered.

One of the most remarkable cases in this group was a woman 60 years of age. She was well nourished, but gave a history of chronic gallbladder disease of several years' duration. The white blood count was 3,000 and the hemoglobin 72 per cent. Typical acute lesions involved the face, the neck, the ears, the arms, the forearms, the wrists, the hands, the legs, and the thighs extensively, and in many areas the lesions were confluent. The temperature had been as much as 100° at times, but she had never been confined to bed. Treatment was started ten months earlier and within three months she was entirely free of the eruption and has remained in good health with a normal blood picture to the present time.

The average duration of skin lesions in this group of cases was thirty-three months. If the case with recurring lesions of fourteen years' duration in which the acute exacerbation had existed only four months should be determined from the time of the dissemination, then the average duration would be twelve months. The shortest duration was two months and the longest two years.

COMMENT

This small group of cases treated over a short time is not sufficient to warrant a definite conclusion. It is not possible to determine when a case of pellagra is entirely cured, since it may relapse even years later. There is also no definite criterion by which to pronounce a case of lupus erythematosus completely cured. The same may be said of some other diseases. So far, the response to liver therapy in the rather acute and widespread type of lupus erythematosus, especially those with definite leukopenia, has been without a doubt more prompt and more satisfactory than from anything tried heretofore. It is hoped that more time and further trial may bear out the excellent response that has thus far been observed.

SUMMARY

This report deals with the use of liver extract in the treatment of eight cases of disseminated lupus erythematosus.

There was complete regression of the skin lesions with restoration of the normal blood determinations, representing good results, in 75 per cent of the cases.

A case with a combination of acute and old discoid lesions had good results in the acute eruption, but there was no effect on the discoid.

Definite improvement was attained in the last case, but the failure completely to recover was attributed to inadequate treatment.

The average treatment time was three months.

The average duration of symptoms was twelve months.

Liver extract is offered as a safe and probably effective measure in the management of disseminated lupus erythematosus.

No established rule of dosage has been followed in this series. The average dose has been 5 to 10 U. S. P. units administered biweekly by intramuscular injection.

BIBLIOGRAPHY

1. Engman, Sr., M. F.: Studies, Observations and Reports from the Barnard Free Skin and Cancer Hospital and the School of Medicine, Washington University, Department of Dermatology, service of Dr. M. F. Engman. Personal communication.
2. Weiss, Richard S.; Lane, Clinton W.; and Bagby, James W.: Effect on the Leukocytes of Therapy with a Gold Preparation. Arch. Dermat. & Syph., **35**:1074-1086 (June) 1937.
3. Hecht, James J.; and Perrin, Samuel R.: The Value of Blood Studies in the Treatment of Lupus Erythematosus. Pa. Med. Jour., **41**:1006 (Aug.) 1938.
4. Ingles, A. E.: Lupus Erythematosus Treated with Sulfanilamide. Arch. Dermat. & Syph., **37**:879 (May) 1938.
5. Abramowitz, E. W., in discussion on Wise, F.: Discoid Lupus Erythematosus Undergoing Dissemination. Arch. Dermat. & Syph., **38**:661 (Oct.) 1938.

6. Belote, G. H.: Lupus Erythematosus Disseminatus. Arch. Dermat. & Syph., **39**:793 (May) 1939.
7. Anderson, H. F.: Fulminating Acute Lupus Erythematosus Cured by Sulfanilamide. Arch. Dermat. & Syph., **38**:621 (Oct.) 1939.
8. Lindsay, H. C. L.: Lupus Erythematosus. Arch. Dermat. & Syph., **39**:888 (May) 1939.

DISCUSSION (*Abstract*)

Dr. Toulmin Gaines, Mobile, Ala.—I do not know how many of you have seen Dr. Harris' exhibit in relation to the etiology of pellagra from defective liver activity. It would be well, after having heard this paper, to look over that exhibit and see how it dovetails into what has been said on this subject. It in a way corroborates the findings of our essayists.

Dr. E. S. Lain, Oklahoma City, Okla.—May I ask what has been Dr. King's experience with liver extract in the fulminating type of lupus erythematosus, or the so-called always fatal type?

Dr. King (closing).—We did not attempt to explain just what liver extract does to the body, because it was more or less accidental in our development of the treatment. It was after use of the drug to build up the blood of one of these patients that we decided to start it on others, especially those with a definite leukopenia and low hemoglobin. We were so pleased with the results that we continued in all the cases of that kind that we could find.

Liver extract was given intramuscularly.

We have not had occasion to see a fulminating case since we started this work. We have hoped that we might see one.

COMMON NUTRITIONAL FALLACIES*

By WILLIAM WESTON, M.D.
Columbia, South Carolina

In order to make the object of this address better understood, I wish at the beginning briefly to discuss the functions of food, the requirements of nutrition and to give a comprehensive definition of nutrition.

The functions of food are: (1) to yield energy; (2) to build or renew body tissue; (3) to regulate body processes and internal conditions in order to maintain a right internal environment for life. These are the functions as described by Sherman. For the purpose of this occasion and in order still further to clarify the subject, I would add a fourth function: to provide for growth and development.

To meet these requirements there must be supplied: (1) sufficient organic nutrients in digestible form to yield the needed energy; (2) protein from a variety of sources sufficient in amount and kind to yield all the essential amino acids that are not synthesized in the body; (3) sufficient amounts in proper proportion of the various mineral elements; (4) sufficient of each of the vitamins in their proper relationship.

There have been many definitions of nutrition, some of them quite lengthy and involved. Consequently we may accept Mendel's terse and comprehensive definition, "the chemistry of life." This definition may seem extravagant unless we recall the statement of McCollum who, after many years of study and investigation, announced: "Food is the determining factor in civilization."

Of the great mass of material that has been published during the past twenty-five years upon problems of nutrition, much is worthless and the remainder of varying grades of importance. When carefully analyzed we may safely conclude that from a variety of natural, properly selected foods all required elements that meet the various demands of nutrition can be readily met without resort to artificial sources.

Much of the material published in the literature announcing sensational discoveries is the result of investigation made from grants by commercial enterprises. Most of them made for commercial purposes, upon investigation, are subsequently found to be inaccurate and are discredited.

Most of the sensational fallacious announcements of discoveries have been made in reference to the mineral elements and less often the vitamins.

It is an accepted truth that life cannot continue to exist unless the diet supplies a sufficient number of mineral elements in proper relation and in sufficient amounts. Until comparatively recently we thought that calcium, phosphorus, potassium, sodium, chlorine, magnesium, sulfur, iodine and iron supplied all the elements essential for normal nutrition. Subsequent investigation has demonstrated that this is far from correct, because we have learned that many of the so-called "trace" elements are likewise essential in the process of nutrition for the maintenance of well-being. Among these may be mentioned manganese, zinc, cobalt, nickle, copper, boron, bromine, silicon, strontium, vanadium, aluminum, fluorine, and arsenic. With the exception of arsenic these elements are invariably found in the tissues and organs of the human being and in no instance has satisfactory proof been offered that any one of them exer-

*Read in Section on Pediatrics, Southern Medical Association, Thirty-Fourth Annual Meeting, Louisville, Kentucky, November 12-15, 1940.

cises a toxic or deleterious influence. On the contrary, several of them have been found to exercise essential functions. It is not improbable that each of them will be found to exercise some definite and useful function in the complicated processes of metabolism. I wish particularly to emphasize the conviction that each of these elements probably has so definite a place in metabolism that when announcement is made by pseudo-chemists that a food contains one of these elements which, under different circumstances, may be toxic, it should be disregarded.

It is manifestly impracticable to discuss on this occasion the functions of each of these elements. Consequently, I shall confine my remarks to a brief discussion of those elements and foods which have been the subject of controversy, much of which has been erroneous and harmful.

In view of the constantly increasing incidence of goiter in the United States in areas where for many years it was not observed, or occurred so occasionally that it might be ignored, we feel that a brief discussion of the element, iodine, is of importance.

We are aware of the fact that in certain localities in which the soil and water are deficient in iodine, there occur many cases of enlarged thyroid gland and a high incidence of feeble-minded children. So serious has been this problem that means for solving it have been sought over a period of many centuries and from time to time it has been thought that the solution had been found. Within the past few years much has been claimed for iodized salt and excellent clinicians have announced that the problem has at last been solved. The observations and examinations by different physicians are so contradictory that we are not prepared to accept their findings. Methods of examination differ materially, which naturally creates confusion. If we are to be open-minded we must give credence to the work of such careful investigators as Lunde, of Norway, and von Fellenberg, of Sweden, who have repeatedly found that when so-called inorganic iodine is ingested in the system all of it is eliminated within twenty-four hours, but that when ingested in its natural relationship as it occurs in foods, it cannot be recovered over a period of weeks. They conclude, therefore, that when ingested in its natural relation, it is either assimilated or stored. Despite these observations the long-continued use of iodized salt in Switzerland, localities in Italy and the United States has resulted in reducing the number of cretins and the incidence of endemic goiter.

McClendon has conclusively demonstrated that in areas where the soil and waters contain a high percentage of iodine and when foods grown in such soils are regularly eaten, endemic goiter does not occur. It has been further demonstrated that regardless of where one lives if foods are eaten which naturally contain a high percentage of iodine endemic goiter will not occur.

There are several localities in the United States that contain a high percentage of iodine and that are suitable for the growing of vegetables and fruits and, with the availability of seafoods that contain a high percentage of iodine, there can be little excuse for the continued existence of this deficiency disease.

It is, moreover, likely that there exist in foods naturally rich in iodine other elements that might be responsible for the utilization of this element in the process of metabolism. It is too often the custom among pediatricians, though they may live in sections in which the soil contains ample iodine, to use the products of other soils that are deficient in iodine in the diets they prescribe. Especially is this true in prescribing green leafy vegetables which are processed in highly goitrous areas and of course grown in soils that are notably deficient in this element. It is our experience from the analyses of thousands of samples of vegetables that it is almost invariably the case when samples are found high in iodine they are also high in iron and that when children are fed on these products they manifest no symptoms of either thyroid enlargement or anemia.

It is a fallacy seriously to consider or to be influenced by the propaganda that your iron requirements should be met by eating raisins or white bread. Both, as a matter of fact, are poor sources of this element. If you are seeking foods that are good sources of iron, you should choose egg yolk, liver, dried beans or peas, whole grain cereals, prunes and green leafy vegetables, such as spinach and kale.

It would be a fallacy to eliminate tomatoes from the diet because they contain copper which, under certain conditions, is a toxic element. In this food and in others as well it serves a useful and highly important function in favorably influencing hemoglobin regeneration.

Among the "trace" inorganic elements, zinc has been ferociously attacked and has been the subject of quite a number of fallacies. Investigations show that zinc occurs in practically all

animal tissue, especially the liver and pancreas, and there are minute traces of it in other organs.

It is most interesting to note that colostrum contains three times the amount of zinc present in normal milk and the zinc content of active glands is twice as high as that of the inactive glands. Scott announces that zinc is a constituent of insulin crystals and he associates this with the presence of zinc in the pancreas, which is relatively abundant. There are various other useful functions ascribed to zinc which need not be reviewed here.

It is a fallacy to assume that food cooked in aluminum ware is in any respect an etiologic factor in cancer or rickets or that as an ingredient of baking powder it is toxic. The truth is that aluminum is universally distributed in soils and plants and even when injected instead of being taken by mouth is not toxic. Aluminum affords another example of the success attained by skilful propaganda. In this case the campaign was conducted by the manufacturers of iron, tin and other wares that had gone into the manufacture of cooking utensils, and these had been largely displaced by aluminum. The battle became so fierce that the British, American and German governments, among others, appointed commissions composed of distinguished groups of chemists to study the effects of cooking in aluminum utensils and to investigate the toxic properties of aluminum. Each of the commissions reported that they could discover no toxic or other harmful influences.

Of all the stupid and fallacious alarms that we can recall was that that we should beware of eating seafood because small traces of arsenic were discovered to be present in fish. The discovery produced great anxiety in many who regularly ate and enjoyed fish from the sea, although none of them experienced arsenical poisoning.

Recently the medical profession and laymen have been frightened by the discovery that spinach contains oxalic acid, which might cause serious interference with the metabolism of calcium. As a matter of fact, oxalic acid occurs in small amounts in a great many fruits and vegetables. Therefore, if we are to eliminate spinach because we fear the formation of calcium oxalates, we should for the sake of consistency eliminate fruits and other vegetables from the diet. You will agree that this would be a serious mistake. Spinach is a vegetable of unusual value on account of its iron content and its ability to bring about quick regeneration of hemoglobin.

Nicotinic acid, the name of which formerly suggested a poison, is beneficial to the body. It is found in plant and animal tissues, and is an essential element to health and life. According to McCollum, "As a portion of the cozymase molecule, nicotinic acid amide became an essential link in the chain of catalysts involved in certain biologic oxidations and reductions." McCollum says also, "It appears, then, that nicotinic acid is either a pellagra-preventive vitamin or a provitamin, or that it is only one, two or more substances for the prevention of this deficiency disease," pellagra.

It is a fallacy to conclude from the erroneous statements that have been made and the high-powered propaganda that has been instituted that oleomargarine is a satisfactory substitute for butter. The manufacturers of this product claim that they have added vitamin A to the product, but they need not claim that they have added other elements that are universally found associated with vitamin A and that may exercise a determining influence upon its ability to function.

It is a fallacy to assume that refined cereals have any useful place in the diet, because in refining cereal grains those portions of the grain that contain practically all of the mineral and vitamin elements are eliminated. Wherever refined cereals have been introduced into the diets of people who have been unaccustomed to their use, there have followed without fail decayed teeth and weak bones.

Sir Edward Mellanby, Secretary of the British Medical Research Council, after a most diligent and careful investigation covering a period of five years, is of the opinion that there is a substance in refined cereals that seriously interferes with the utilization of calcium. It is usually a fallacy to assume that brown colored bread is whole wheat bread, as it usually is nothing more than white flour to which has been added brown coloring matter.

May I assure you that it is a fallacy to believe that there exists a perfect substitute for mother's milk. No one has ever discovered the secret of

adding the biological elements of human milk to any other kind of milk.

Due to high-pressure advertising, we are constantly hearing from mothers that they add to the baby's milk formula "cocoa malt" or "ovaltine" for the improvement of the baby's appetite and to overcome restlessness. Usually when such cases are investigated it is found that refined cereals are regularly supplied in the diet and that this is the source of loss of appetite and restlessness. It is a fallacy to believe that these preparations can supply the deficient elements or that they add anything to the diet that cannot be more cheaply and advantageously supplied from natural foods.

In order that I may not leave any misapprehension as to my object in presenting this paper, I wish it understood that it is my opinion that when any chemical element is regularly found in the tissues or glands of the body and also in edible plants or foods, this element should not be the object of suspicion. In all probability it serves a definite function in the processes of metabolism.

DISCUSSION (*Abstract*)

Dr. J. K. Mack, Louisville, Ky.—I should like to emphasize a statement in Dr. Weston's paper, that from a variety of natural, properly selected foods all nutritional requirements can be readily met without resort to artificial sources.

We all know that there are a number of foods which lately have come into disuse, for example, beans. Beans are a very good food from a nutritional standpoint. Dr. Weston mentioned whole grain cereals. Whole wheat bread is not used nearly so much as it should be. A number of us still believe that cod liver oil is probably a better source of vitamins A and D than the concentrates. We believe that something is supplied in cod liver oil that is not supplied in the concentrates. If we believed the drug salesmen we should assume that we may eat meat and potatoes and probably some bran, and take one little brown polysyllabic pill and fulfill all the nutritional needs. I think that we should start a counter propaganda campaign to increase consumption of the neglected foods, which are nutritionally valuable, particularly the whole grain cereals and whole wheat.

Dr. Seale Harris, Birmingham, Ala.—Physicians are responsible for the ill use of the concentrated, synthetic vitamins that Dr. Weston spoke of, and there are a hundred times as many vitamins prescribed as there are indications for their use. Physicians are prescribing vitamin preparations under trade names without really knowing what they are giving.

McCollum's new book on nutrition, the fifth edition, contains more information on vitamins than any book that has been published. McCollum says, like Dr. Weston, that vitamins should be obtained in foods, and that expensive synthetic vitamins are valuable only in emergencies. As Dr. Weston says, it is rarely necessary to use store-bought vitamins. A recent number of *Hygeia* contains one of the best articles that I have seen entitled "Vitamin Crazy." There is a drug store right across from my office, and one day I asked the druggist how many vitamins he was selling on doctors' prescriptions and how many to the public. He said: "We sell ten times as many vitamins over the counter as we sell on prescriptions."

Dr. Weston has been working on iodine in food for a great many years. He has brought out some very valuable facts, and the people of South Carolina think so much of Dr. Weston that they now call South Carolina the "iodine state." I am inclined to think that there must be something in the vegetables and other foods that are grown in the soil of South Carolina that produce men like Marion Sims, John C. Calhoun, the elder Hayne, and I may add Dr. Hayne, the State Health Officer of South Carolina, and men like Dr. Weston and Dr. Wilson and the other men whom we know in South Carolina. We shall have a super race of people in the next generation if high-pressure salesmen do not get out too much propaganda and induce people to use too many of the concentrated vitamins. McCollum's dictum upon eating is this: every child should have a quart of milk, one raw fruit, one raw vegetable, one or two cooked green and yellow vegetables a day, meat probably once a day, and enough bread made from whole grain cereal to give him energy and to maintain body weight. The super race will come when all men, women and children live on the simple diet suggested by McCollum.

I have used many of these synthetic vitamins. There never has been a case of pellagra cured with yeast, nicotinic acid, liver or anything else without improvement in the patient's food. Of course, nicotinic acid should be given for a few days in beginning the treatment of pellagra, but one must improve the nutrition of the pellagrin by giving him the proper food if he is to be cured of pellagra permanently.

Dr. Weston (closing).—I am a great dog fancier, and I have found that I can give corn meal to my dogs every day for a week and at the end of that time every dog will have a red mouth and a red tongue. On my farm I have undertaken other experiments with animals. If I feed a sow every day on white bread she will not become pregnant. If, under other circumstances, the sow does become pregnant, if I give her white bread every day for a week she will abort.

Among pediatricians, the one complaint that we hear most often is of restlessness, loss of appetite, and sleeplessness of babies. If we put the baby on unpolished rice for just a few days those symptoms will promptly disappear, because in the vitamin B complex there are not just four or five elements, but probably several hundred elements, and the number of symptoms that a deficiency of these elements produces runs into the thousands; but from that one source we can obtain in a perfectly satisfactory form all the B elements, and we get them in their natural, proper relationship.

OPERATION FOR RELIEF OF ASCITES IN HEPATIC CIRRHOSIS*

By THOMAS O. OTTO, M.D.
Miami, Florida

The condition of ascites (abdominal dropsy) was known to the ancient Romans. Vesalius noted the wasted liver of drunkards. Matthew Baille[1] first associated dropsy with shrunken liver. Laennec is recognized as the father of the disease, and first used the term cirrhosis, meaning yellow.

Alcohol is not a necessary factor in causation, but frequently is present. It is regarded as merely a noxious influence on the liver.

Fagge[2] has shown that portal cirrhosis is frequently associated with ascites, but ascites may be totally lacking in advanced cirrhosis.

Hepatic cirrhosis must be regarded as one form of portal venous obstruction which can produce ascites. Extrahepatic portal obstructions commonly cause ascites, such as carcinoma in the head of the pancreas and other abdominal malignancies with metastatic strangulation of the portal vein.

Any portal vein obstruction, whether producing the condition of ascites or not, can cause hematemesis and bleeding from the bowel, one of the first signs in the diagnosis after the silent stage of cirrhosis. This phenomenon is readily explained on the basis of the portal venous tributaries lying anatomically nearer the mucosa than the serosa.

Portal cirrhosis must be regarded as an intrahepatic obstruction to the portal vein producing a hypertension in the portal system and resulting in ascites, splenomegaly and melena. Recently, Rousselot[3] has presented fifteen cases in support of chronic portal obstruction as a precursor of splenomegaly, and the clinical picture of Banti's syndrome in late stages without cirrhosis, proving a mechanical factor as the true etiology rather than a hypothetical toxin. Rousselot[3] has proven all cases by biopsy of the liver and histologic examination in ten of the fifteen cases reported.

Other commonly known causes of ascites are abdominal tuberculosis, lues, and polyserositis.

Bowman[4] has shown the accuracy of the bromsulphalein test in the diagnosis of hepatic damage; and it is interesting to note that in the cases of Rousselot no discrepancy between the clinical test of liver function and biopsy and autopsy findings was encountered.

In reviewing the literature of many authors on the surgical treatment of ascites, and noting the marked variation in types of cases reported in which, at autopsy, the diagnosis of true portal cirrhosis failed to be proven, it is this author's opinion that the positive diagnosis of portal cirrhosis can be made only by biopsy on the liver.

Henrikson[5] has ably classified the surgical procedures advanced for the relief of ascites. These procedures are ingenious, numerous, and varied as to approach and magnitude. The great variety of procedures indicates that no particular method has been satisfactory. Some procedures are directed toward the establishment of permanent drainage, with permanent loss of the ascitic fluid, for example, paracentesis abdominalis; permanent fistula between abdominal cavity and bladder; and permanent indwelling glass tube between abdominal cavity and the exterior. These have all proven to be unsatisfactory, leading to eventual fatal peritonitis and hypoproteinemia, with possibly the exception of paracentesis, popularized by Höpfner, from which as many cures have been reported as from any other one method. Weber[6] says that the cures following repeated paracentesis are probably due to the formation of omental adhesions and the gradual development of collateral circulation at the sites of puncture, and the inevitable peritonitis following repeated puncture. Riesman[7] reports a case in which paracentesis was performed thirty-six times, with a total of 150 gallons removed. Fibrinous peritonitis developed after the last time, and the patient was cured of ascites.

Other procedures for the relief of ascites have been directed toward drainage of the ascitic fluid into the subcutaneous tissues, as accomplished by Handley through the femoral canal, and by Boccaro and Tannehill through the use of a collar button glass tube extending from the peritoneal cavity into the subcutaneous fascia.

Surgical attempts to drain the ascitic fluid directly into the systemic circulation by means of the saphenoperitoneal anastomosis of Ruotte,[8] popularized by Miller[9] in this country, were well received, but the method failed of its purpose because of venous obliteration by the action of the ascitic fluid.

Other surgical procedures have consisted of

---

*Read in Section on Surgery, Southern Medical Association, Thirty-Fourth Annual Meeting, Louisville, Kentucky, November 12-15, 1940.

venous anastomoses designed to short-circuit the liver and lessen the portal hypertension; and in this group is the classical attempt at anastomosis between the portal vein and inferior vena cava, the so-called Eck's fistula, rarely attempted, and, disregarding its formidable nature, found to end fatally, with all patients dying in toxemia resembling uremic coma. This result would be expected in view of the digestive products passing directly into the systemic circulation without being subjected to the detoxifying action of the liver. Other venous anastomoses have been performed, namely, the superior mesenteric and the inferior vena cava, and the superior mesenteric and ovarian or spermatic veins, but here one would expect the same result.

Lord Moynihan has practiced ligation of the inferior mesenteric, and C. H. Mayo the inferior mesenteric and superior rectal veins, to hasten collateral circulation and diminish the portal stream to the liver.

Regarding all procedures, the most satisfactory results have been accomplished by those in which the collateral circulation has been improved. These procedures have been omentopexy and visceropexy or a combination of both. Omentopexy in some form has given most satisfactory results.

Mayo[10] says:

"The extent of collateral circulation established in this way is extraordinary. In several cases I made the incision for other purposes (after omentopexy), but encountered so much bleeding I had to desist."

The familiar Talma-Morrison procedure has been most often used, and Schiassi[11] has modified this procedure by implantation of the omentum between the peritoneum and posterior surface of the abdominal parietes.

Narath has transplanted the omentum into the subcutaneous tissues of the abdomen through to the rectus muscle.

Turner has interposed the omentum between the liver and parietes.

It is a common surgical finding that the omentum, under traction or compression, or both, loses its integrity and becomes avascular and fibrotic. It therefore appears that omentopexy without transposition or compression, or placing the omentum under traction, would best serve to establish collateral circulation.

Hughson[12] has stressed the frequent finding of a markedly thickened peritoneum in the presence of chronic ascitis and comments on its nonabsorbing and fibrotic quality.

The operation I wish to report at this time is based upon the observations of Hughson,[13] who says:

"A constant operative finding has been the presence of a markedly thickened peritoneum. Simpson draws attention to this fact, and states that most cases show a chronic peritonitis. It is probably safe to go further and say that all cases of any particular duration exhibit a chronic peritonitis. The peritoneum normally absorbs fluids rapidly. The thickened peritoneum of a portal cirrhosis could not possibly absorb and undoubtedly plays a fairly important part in elaborating the fluid. Might it not be reasonable, therefore, to explain possible benefit obtained from surgical intervention on the basis of obliteration of the peritoneal cavity, from whatever cause, rather than from the establishment of a doubtfully adequate collateral circulation. As a possible form of treatment, removal of large areas of parietal peritoneum suggests itself for the surgical obliteration of the peritoneal cavity without having recourse to infection."

This operation embodies the principle of extensive excision of the thickened peritoneum, and allows the omentum to remain in its normal position without compression or traction. The technic is simple and carried out without shock. It affords exploration of the abdominal cavity and permits of scrubbing the liver with dry gauze, as commonly practiced in the classical Talma-Morrison procedure. It affords biopsy of the liver, which is the only positive diagnosis of portal cirrhosis.

This operation is performed under local infiltration anesthesia, 1 per cent procaine hydrochloride, through a long right rectus incision carried inward to the peritoneum. At this point, supplementary gas anesthesia, cyclopropane, is administered. The peritoneum is mobilized laterally with the gloved hand so far as permitted before entering the peritoneal cavity. Care is exercised to avoid rupture of the dilated vitelline veins coursing through the round ligament toward the umbilicus. Bleeding has not been found serious, being controlled by warm, wet Mikulicz pads. A stab incision is now made through the peritoneum and the fluid removed as completely as possible by aspiration.

The peritoneal incision is lengthened to correspond to the skin incision and the abdomen thoroughly explored.

In the absence of any organic cause for the ascites except liver disease, a biopsy is taken from the liver margin. The liver surface is rubbed with dry gauze to aid adhesions. The omentum is left in its normal anatomical position. The abdominal wall is retracted upward and outward, and the large peritoneal leaflets, previously formed by mobilization, are removed

with scissors under direct vision. The amount of peritoneum excised is dependent upon the size of the abdomen. The excision is carried lateralward to a point medial to its reflexions over the ascending and descending colon. It is cut away in a downward direction and then joined medially by cutting transversely approximately one inch above its beginning reflexion over the bladder. An attempt is made to excise the entire anterior parietal peritoneum of the abdominal wall. The abdomen is closed with interrupted No. 16 gauge silver wire sutures, threaded on a curved cutting Mayo needle, and laid approximately 1.5 cm. apart. These are lifted upward and twisted and juggled so as to bring all the remaining layers of the abdominal wall into normal juxtaposition. Healing is complete and secure and the sutures are removed at three weeks.

This operation has been done successfully three times, without shock, without secondary hemorrhage, and without intestinal obstruction. The failure of intestinal obstruction to develop is most likely explained by the adhesions of the omentum to the denuded anterior parietes, and the fact that the intestine in coming into contact with the abdominal wall presents itself with the antimesenteric surfaces to the denuded parietes. If adhesions do occur, they would serve likewise to further the desired collateral circulation.

Postoperative paracentesis has been necessary but two or three times in this brief series of cases. This has been performed at weekly intervals and collateral circulation has been found to be estabished in three weeks, and ascites has not recurred.

Following is a brief clinical synopsis, together with results, of three cases operated upon by this method:

Case 1.—J. R. P., a white man, aged 39 (Union Memorial Hospital, Baltimore, Path. No. 2530) was admitted to Union Memorial Hospital from Johns Hopkins Hospital with complete clinical study and diagnosis of alcoholic cirrhosis with ascites. Paracentesis had been performed nine or ten times prior to his admission at Hopkins, and on an average of every three weeks, 6,000 to 18,000 c. c. of ascitic fluid were being removed at each tapping. After seven paracenteses, between August and November of 1928, at Union Memorial Hospital, this operation was first performed on November 28, 1928. Diagnosis was confirmed by biopsy of the liver. Postoperative paracentesis was performed three times with an average of 5,000 to 7,000 c. c. removed at each tapping. From January, 1929, until November, 1932, no ascites recurred. The family physician at Java, Virginia, reported death to have resulted from cardiac failure and generalized edema in November, 1932.

Case 2.—D. S., a white man, aged 65 (Case 49876, Jackson Memorial Hospital, Miami, Florida), a chronic alcoholic, was admitted to the hospital six times for paracentesis. The clinical diagnosis was cirrhosis of the liver with ascites. He was operated upon November 15, 1932, by the method described in this paper. The clinical diagnosis is confirmed by biopsy. Paracentesis was done twice postoperatively, with an average of 3,000 c. c. of fluid. He had good health for four years and ten months. No ascites recurred during this period. He was readmitted October 14, 1937, with clinical signs of intestinal obstruction. At the operation, peritonitis, due to perforation of the descending colon produced by a foreign body, was determined to be the cause of death November 1, 1937.

Autopsy showed macroscopically and microscopically moderate cirrhosis of the liver, and peritonitis due to perforation of the colon by a foreign body.

Case 3.—E. J., a white man, aged 55, Jackson Memorial Hospital, Miami, Florida (Path. No. 8368), a chronic alcoholic, had a clinical diagnosis of hepatic cirrhosis with ascites. Paracentesis was done twice preoperatively and approximately 2,000 c. c. were removed at each tapping. He was operated upon August 31, 1940, by the method described in this paper. The preoperative diagnosis was confirmed by biopsy. The patient survived sixty-six days, developed septicemia and expired November 4, 1940.

Autopsy showed ascites, cirrhosis of the liver and pulmonary abscess. The cause of death was septicemia.

SUMMARY

(1) The surgical procedures for relief of ascites have been briefly reviewed.

(2) The operation presented is simple in performance and permits of positive diagnosis by biopsy of the liver and thorough exploration of the abdominal cavity. It is attended by minimal operative risk.

(3) Results in this brief series have been eminently satisfactory in relieving the ascites, and in returning two of the three patients to their normal activities.

BIBLIOGRAPHY

1. Moynihan, Sir Berkeley: Abdominal Surgery, vol. 2, chapter 47. Philadelphia: W. B. Saunders Co., 1926.
2. Fagge, Charles Hilton: Principles and Practice of Medicine. Quoted by Moynihan.[1] Philadelphia: P. Blakiston's Son & Co., 1886.
3. Rousselot, Louis M.: Late Phase of Congestive Splenomegaly (Banti's Syndrome) with Hematemesis but Without Cirrhosis. Surg., **8**:34 (July) 1940.
4. Bowman, L.; and Orr, L.: N. Y. State Jour. Med., **38**:17, 1938.
5. Henrikson, E. C.: Arch. Surg., **32**:413-51, 1936.
6. Weber, F. B.: Hepatic Cirrhosis and the Question of Operative Treatment of Chronic Ascites. Int. Clin., **1**:88, 1924.
7. Riesman, D.: Spontaneous and Operative Cure of Cirrhosis of the Liver. J.A.M.A., **76**:288 (Jan. 29) 1921.
8. Ruotte: Lyon Med. Jour., **109**:574, 1907.
9. Miller, R. T.: Penn. Med. Jour., **19**:413 (March) 1913.
10. Mayo, W. J.: Surgical Treatment of Hepatic Cirrhosis. Ann. Surg., **80**:419, 1924.
11. Schiassi, B.: Semaine Med., **21**:145, 1901. La deviation Chirurgicale du sang de la veine porte.
12. Hughson, Walter: Portal Cirrhosis with Ascites and Its Surgical Treatment. Arch. Surg., **15**:418-440 (Sept.) 1927.
13. Hughson, Walter: Int. Surg. Digest, **5**:131-138 (March) 1928.

DISCUSSION (*Abstract*)

Dr. H. Hart Hagan, Louisville, Ky.—Dr. Otto offers another possibility in the treatment of a condition that has not been successfully treated in the past.

We might deplore the fact that there has not been greater opportunity for investigation in these cases, but there is possibly not much encouragement to medical men to refer these cases in any considerable number for major surgical relief.

It is a fact that paracentesis gives palliative relief in a large percentage of cases, and it is also most interesting to know that paracentesis has been accompanied by permanent relief in a few isolated cases. We may well ask ourselves why this has happened.

It is possibly due to the fact that there has been produced a low-grade peritoneopathy, possibly, by the repeated trauma, so Dr. Otto's suggestion commends itself because it offers an opportunity for positive diagnosis by biopsy from the liver. Most writers have emphasized the fact that we should always avail ourselves of this opportunity.

It is perfectly possible that the cures that have been claimed for some of the other methods are due in large part to treatment under mistaken diagnosis. Further, this method offers a removal of a rather large extent of the peritoneum, and diseased peritoneum at that.

As Dr. Otto has indicated, peritoneum is usually found to be thickened, probably from low-grade peritonitis, and it is a well-known fact that peritoneum that is diseased and thickened fails to perform its usual function. In other words, it is likely to become an exudative membrane rather than absorptive.

It is even possible that this thickened membrane plays some part in the production of fluid which we find in the abdomen. Furthermore, this method offers an opportunity for free education between the omentum and the abdominal wall without traction, without compression and without the production of extensive fibrosis.

And furthermore, this is an operation that is easily performed and performed under simple anesthesia locally, followed by gas, so it is to be hoped that Dr. Otto may be afforded an opportunity further to investigate these cases.

Dr. Guy Aud, Louisville, Ky.—Dr. Otto's operation for ascites following cirrhosis of the liver is, to me, the most logical procedure yet devised for the relief of this distressing condition. In order to relieve the ascites resulting from obstruction of portal circulation incident to hepatic cirrhosis it is necessary to produce peritoneal adhesions over a very large area in order to establish an adequate collateral circulation.

The operation of Dr. Otto accomplishes two very important things: first, it removes a very large area of secreting peritoneum. While it is true that this area is very small in comparison to the total peritoneal surface, it is, nevertheless, of considerable consequence. Secondly, it creates the largest possible area for the establishment of adhesions and collateral circulation.

There are two possible objections, or I might say dangers, of this operation that occur to me at this time. One would expect intestinal obstruction to follow more frequently than would seem to be indicated in this report and one cannot help but wonder what difficulties he would encounter should it become necessary to reopen such an abdomen.

Dr. J. M. Frehling, Louisville, Ky.—In the selection of an operative procedure, one is primarily concerned with the establishment of a normal anatomical relationship and with the restoration of function. It is for this reason that I wish to call attention to the fact that in his report the speaker failed to emphasize what to me seems of primary importance. Men suffering from ascites due to hepatic cirrhosis are almost invariably chronic invalids. To be able to restore these individuals to normal usefulness would be, of course, most gratifying.

The many operative procedures heretofore recommended for the relief of this condition have had restoration of function as their ultimate aim. In the cases reported, exclusive of the one that died, Dr. Otto has succeeded in returning these men to their former occupations to a degree approximating their former usefulness.

This strikes me as being the important feature of his contribution. Not only was the ascites relieved, which in itself is relatively unimportant, but by means of a relatively simple operative procedure, easily executed. The subject has gained a new lease on life and that feature alone is sufficient recommendation for Dr. Otto's operation and cannot, I think, be overemphasized.

Dr. L. Wallace Frank, Louisville, Ky.—Dr. Otto described the autopsy findings in his cases, but he made no mention of the extent of adhesions of the omentum to the anterior abdominal wall. After all, that is what we are interested in; also, whether or not it occurs between the intestine and the anterior abdominal wall, and whether there was any attempt at regeneration of the peritoneum, because we know that it does have a tendency to regenerate.

Dr. Otto (closing).—First, allow me to apologize for the brevity of this series of cases reported, and the long period of time in which they were performed.

There are two principal reasons for the shortness of the series: first, the hospitals of Miami do not afford a large number of these cases; second, advanced cases of ascites are as much the legitimate prey of the medical man as they are of the surgeon; and as long as they remain a source of revenue for repeated tapping, it is difficult for me to get hold of them for what we might call experimental purposes.

In regard to the results in the three cases reported, and the condition following this operation, allow me to summarize briefly: The first patient survived four years and ten months without ascites and was actively engaged in truck farming for this period of time. He died of a cardiac complaint, and a letter from his family physician at Gretna, Virginia, said that he did not develop ascites. No autopsy was performed in this case.

The second case survived a period of five years and engaged as a contractor-builder for a period of five years. During this time he continued to drink beer, reported frequently to my office, and at no time developed the slightest evidence of ascites or obstruction. Prior to this operation, he had suffered a large indirect inguinal hernia on the right side. No attempt at herniorrhaphy was made, but following the removal of the ventral peritoneum his hernia was cured, as well as the ascites. This patient was admitted to the hospital after five years, in practically a moribund condition, with a diagnosis of intestinal obstruction. He had been treated elsewhere for practically a week, and I attempted en-

trance to the abdomen through a left rectus incision. Laparotomy was extremely difficult. The patient was found to have suffered from a foreign body (chicken bone) perforation of the descending colon at its mid portion, and was dying from an extensive but localized peritonitis. Complete exploration of the abdomen could not be done at this time. Drainage was instituted after closure of the perforation, and this man died after a few days of peritonitis.

Autopsy in this case revealed extensive adhesions between the omentum and parietes; and adherent loops of intestine to the abdominal parietes, but no evidence of obstruction could be found, although it was carefully searched for.

Case three of this series survived sixty-six days postoperatively, with a normal convalescence, secure healing of the abdominal wall, and no recurrence of ascites. Occasional attacks of melena and hematemesis continued. After seven weeks, he developed a fatal septicemia and died on the sixty-sixth postoperative day.

Autopsy revealed extensive abdominal adhesions, no obstruction, no ascites, and a well established collateral circulation. An unsuspected pulmonary abscess in the lower left lobe was encountered, from which he probably developed his fatal septicemia.

The patients with ascites in hepatic cirrhosis are poor surgical risks. The autopsy findings in cases two and three, briefly summarized above, would indicate that postoperative obstruction is not greatly to be feared. The three cases reported have survived operation without shock and without recurrence of ascites, with only one fatality resulting from complicating pulmonary abscess and septicemia.

I hope to add to this series, but I hope more strongly that other men will try this operation in these invalided and otherwise hopeless surgical cases.

UTERINE BLEEDING FROM THE VIEWPOINT OF THE OBSTETRICIAN*

By NICHOLSON J. EASTMAN, M.D.
Baltimore, Maryland

The common causes of obstetric hemorrhage, in the approximate order of their frequency, are: postpartum hemorrhage, abortion, placenta previa, ectopic pregnancy, premature separation of the normally implanted placenta and rupture of the uterus. As an immediate cause of death in childbirth, obstetric hemorrhage ranks second both to puerperal infection and the toxemias of pregnancy. Thus, of 10,585 carefully studied maternal deaths compiled from representative American sources, 39.1 per cent were due to puerperal infection, 22.4 per cent to toxemias, and 18.1 per cent to hemorrhage.

As a contributory cause of maternal death, hemorrhage exacts an important additional toll, but one which is difficult to evaluate with precision. The evidence indicates, however, that if all the deaths in which hemorrhage plays a part were grouped together, the total number would exceed those due to the toxemias and almost equal those ascribable to infection. This statement is based on the following considerations: (1) Hemorrhage predisposes to puerperal infection. Among 1,290 consecutive cases delivered on the Bellevue Obstetrical Service and reported by Reich, the morbidity in 1,154 cases in which there was no postpartum hemorrhage was 15.1 per cent, whereas in 136 cases of postpartum hemorrhage it reached 41.9 per cent. Similarly, Pastore has observed a definite increase in postpartum fever with increase in blood loss. (2) Hemorrhage predisposes to shock, a fact too well known to need statistical substantiation. (3) Many of the procedures employed in the treatment of severe hemorrhage, such as manual removal of the placenta and uterine tamponade, introduce infection, inflict shock and often require prolongation or renewal of anesthesia.

The relative frequency of the common causes of death from obstetric hemorrhage is shown in *Table 1*. It is apparent that limits of time preclude our discussing, even in outline form, these six conditions, which run very nearly the whole gamut of obstetrics. Accordingly, with your permission, I shall touch very briefly upon but one or two small phases of each of these complications.

Postpartum Hemorrhage.—One of the most valuable methods of controlling postpartum hemorrhage is seldom used in this country, namely, bimanual compression of the uterus. It is carried out as follows: insert one hand into the vagina, close it, making a fist with the back of the hand directed posteriorly and the knuckles in the anterior fornix; put the other hand on the abdomen, resting on the posterior surface of the uterus, and press the anteverted uterus down onto the fist by the external hand. In this way the posterior wall is pressed against the anterior, and hemorrhage checked; constant rotation of the internal hand, moreover, gives the uterus most effectual massage. Described first by Hamilton in 1861, bimanual compression of the uterus is the usual method of treating severe postpartum hemorrhage in England, but elsewhere has not received the attention it deserves. It can be

---

*Read in Joint Session, Section on Gynecology and Section on Obstetrics, Southern Medical Association, Thirty-Fourth Annual Meeting, Louisville, Kentucky, November 12-15, 1940.

*From the Department of Obstetrics, the Johns Hopkins University and Hospital.

Table 1

INCIDENCE AND COMMON CAUSES OF FATAL OBSTETRIC HEMORRHAGE BASED ON 10,585 MATERNAL DEATHS

	Children's Bureau Study	New York Study	Philadelphia Study	Maryland Study	Total
Total deaths	7380	2041	717	447	10,585
Deaths due to hemorrhage	1368	361	122	73	1,924
Per cent due to hemorrhage	18.5	17.2	17.0	16.5	18.1
Classification of Hemorrhage					
Postpartum hemorrhage	374	117	27	21	539
Per cent of hemorrhage deaths	27.3	32.4	22.1	28.8	28.0
Placenta previa	347	49	23	25	444
Per cent of hemorrhage deaths	25.4	13.6	18.9	34.2	23.1
Ectopic pregnancy	249	72	25	9	355
Per cent of hemorrhage deaths	18.2	19.9	20.5	12.3	18.5
Abortion hemorrhage	254	27	15	7	303
Per cent of hemorrhage deaths	18.5	7.5	12.3	9.5	15.7
Rupture of uterus	74	65	20	3	162
Per cent of hemorrhage deaths	5.4	18.0	16.4	4.3	8.4
Premature separation	70	31	12	8	121
Per cent of hemorrhage deaths	5.1	8.6	9.8	10.9	6.3

carried out more quickly than uterine tamponade, requires no special apparatus, is much less likely to introduce infection and in my own experience is more efficacious.

Placenta Previa.—It has long been a maxim of obstetrics that vaginal bleeding in the last trimester of pregnancy calls for immediate vaginal examination in order to establish or rule out the diagnosis of placenta previa. Since this procedure entails insertion of the finger through the cervix and palpation of the area immediately surrounding the internal os, its dangers are obvious, namely: precipitation of fresh hemorrhage, introduction of infection and initiation of premature labor. Because of these drawbacks, various investigators have explored the possibility of employing the x-ray for this purpose. During the past two years, Dippel and Brown, of our clinic, have used soft tissue roentgenography on over 200 pregnant women, of whom approximately one-quarter were x-rayed because of bleeding in the last trimester. The placenta was clearly visualized in about 90 per cent of the cases. Contrary to general opinion, good soft tissue work can be done on a simple portable x-ray apparatus, and should be possible in any hospital with a roentgen equipment. A single lateral roentgenogram is usually sufficient. The chief value of the method lies in its ability to rule out placenta previa with complete certainty, so that a substantial number of women who bleed in the last month of pregnancy may be spared vaginal and cervical exploration.

Present day trends in the treatment of placenta previa may be summarized as follows: (a) The liberal use of blood transfusion is prerequisite to the successful outcome of any form of treatment. (b) Rectal examinations are inconclusive and dangerous; sterile vaginal examinations should be done only after the operating room is set up for the immediate institution of any form of treatment that may be indicated, including cesarean section. (c) Provided the patient is not infected, all cases of central placenta previa and all cases of partial placenta previa in primigravidae are best treated by cesarean section. (d) Most cases of marginal placenta previa in multiparae are best handled by rupture of the membranes. (e) In cases which fall between the two extremes mentioned in "c" and "d," the present trend is toward cesarean section. (f) Concerning the relative value of

classical and low cervical cesarean section, opinion is divided; if the placenta lies anteriorly, most authorities favor the classical operation.

Ectopic Pregnancy.—In 1891, Schauta demonstrated that prompt operation in ectopic pregnancy had reduced the mortality from 86.9 to 5.7 per cent. Today, almost fifty years later, it is disappointing to record that our results are only slightly better than in Schauta's time. In a series of 3,343 American cases collected from the literature between 1925 and 1935, Gordon found an average mortality rate of 4.6 per cent. Tardy recognition of the condition, followed by a tardy operation, is responsible for the majority of these deaths. With the exception of pain, no single symptom of ectopic pregnancy is present in more than 90 per cent of cases; no single physical finding is present in more than 85 per cent, while the leukocyte count may range from 5,000 to 25,000. The classical picture of ectopic pregnancy is observed in a small minority of cases only, whereas the most frequently seen case is the atypical one. Every woman in the child-bearing period who has lower abdominal pain must be studied with wary alacrity if we are to carry out prompt operation for this condition, which still carries a high death rate.

Abortion Hemorrhage.—In regard to bleeding from abortion, it is the consensus of opinion that continuous bleeding, exceeding that of menstrual flow, necessitates evacuation of the uterus, but the tactics employed will vary with the presence or absence of infection. Even in the absence of infection, most authorities recommend either digital evacuation or the employment of a dull curette, but it is my opinion that in a clean case better results are achieved by the use of a rather large, sharp curette. Intelligently handled, the sharp curette is preferable to the dull instrument because it is less likely to slip over adherent placental fragments. In the presence of infection, the simplest method which will control the bleeding is the best, intra-uterine manipulation being avoided if at all possible. The common procedures employed to meet this situation are: (a) The administration of posterior pituitary extract in an effort to obtain spontaneous expulsion of the uterine contents. (b) Inspection of the cervix, which will often be found dilated with the product of conception in its rim, whence it can be easily removed without uterine invasion. (c) If the above measures fail, uterine tamponade must be resorted to, the gauze being removed after twelve hours; following this period the product of conception is ordinarily completely separated and is either in the vagina or can be removed from the uterus without extensive uterine manipulation.

Rupture of the Uterus.—It is important to recall that rupture of the uterus can occur without dramatic phenomena. It is my experience that shock is to be expected in only half of the non-cesarean cases and still less frequently in post-cesarean ruptures. Some years ago, at the Johns Hopkins Hospital, a patient walked into the prenatal clinic with rupture of a cesarean scar. During the past four years I have seen three cases of spontaneous rupture in normal multiparae after periods of labor which were less than twelve hours, and in two of the patients there was neither shock nor appreciable abdominal tenderness. In the third case, a fatal one, bleeding and shock followed the spontaneous delivery of a large baby; the diagnosis was postpartum hemorrhage until postmortem exploration of the uterus revealed an extensive rupture. It is my opinion that rupture of the uterus is a more common cause of maternal death than ordinarily believed and that not a few of the deaths charged on birth certificates to postpartum hemorrhage belong in this group.

Premature Separation of the Normally Implanted Placenta.—If patients with premature separation of the placenta are already in labor, it is our custom to deliver them vaginally with the help of artificial rupture of the membranes and an abdominal binder. If they are not in labor and exhibit a clear-cut case of the disorder, we employ cesarean section, but insist that blood be running into the vein before the operation is started. We believe that this employment of blood transfusion, during the operation, meets the main objection to this form of treatment, namely: imposition of major surgery on an already shocked patient. Here, as in all forms of obstetric hemorrhage, blood transfusion may be a life-saving measure and, indeed, must be regarded as our most important single bulwark against this whole group of conditions.

Discussion follows paper of Dr. Novak, page 416.

GENITAL BLEEDING FROM THE GYNECOLOGIST'S VIEWPOINT*

By RICHARD W. TELINDE, M.D.
Baltimore, Maryland

In speaking of genital bleeding from the viewpoint of the gynecologist, I will speak only of the organic lesions responsible for this symptom. This is not to say that the gynecologist is not interested in functional uterine bleeding, but that phase of the subject will be covered by Dr. Novak in this symposium. Functional bleeding may be slight or may be very profuse and, at times, may be responsible for a grave anemia. Bleeding from an organic lesion, likewise, may be slight or profuse, and one should always bear in mind that there is no relation between the amount of flow and the seriousness of the lesion. Not infrequently a slight intermenstrual spotting may be a manifestation of the gravest of lesions.

The age factor is a most important one in considering genital bleeding. In the teens, bleeding is almost always functional. In the third decade of life, bleeding is also usually of a functional nature if one excludes that associated with pregnancies. Pelvic inflammatory disease, however, represents one organic lesion which is often associated with bleeding in the twenties. In the fourth decade, the incidence of functional bleeding is definitely on the decline, but myomata and cervical carcinoma assume important roles in causing bleeding. In the fifth decade of life, functional bleeding again increases greatly; in fact, it is during this period, just before and during the menopausal years, that functional bleeding has its greatest incidence. But this decade is also the time of greatest incidence of bleeding from cervical carcinomata and uterine myomata. After the menopause, genital bleeding is almost always due to organic causes. Not only is the postmenopausal lesion an organic one, but in more than half the cases malignancy of some part of the genital tract is responsible.

In my limited time I shall consider bleeding only from the standpoint of diagnosis of the underlying pathologic lesion. This is the real problem that confronts the pnysician and it is in the making of this diagnosis that the most serious mistakes occur. Once the pathologic nature of the lesion has been determined, the indications for treatment are usually clear. I shall discuss briefly the commoner lesions causing bleeding, beginning at the vagina and progressing up the generative tract.

Ulceration from an ill-fitting or neglected pessary often causes bleeding from the vaginal wall. At times excessive granulation tissue is produced which may suggest the possibility of vaginal carcinoma. This latter lesion is rare, but if there is any suspicion of it the tissue should be biopsied.

After the menopause the withdrawal of the estrogenic hormone results in a very thin vaginal mucosa which easily becomes superficially ulcerated in small areas. The ever-present vaginal flora penetrates the tissue in these areas and vaginitis results. The milky discharge is often tinged with blood, but seldom does frank bleeding occur unless there is adhesion formation between the walls of the vagina. When these adhesions are ruptured they may cause more profuse bleeding.

The cervix is a very common source of hemorrhage. With marked prolapse ulceration is frequent. Again this usually produces a blood-tinged discharge rather than frank hemorrhage. With bed rest and douching these ulcerations usually heal promptly. If they do not, a biopsy should be done before surgery is attempted for the prolapse.

Cervical polyps are among the common lesions causing bleeding. It is usually slight, often preceding or following menstruation or occurring without relation to the period. A history of spotting following coitus, defection or any strenuous physical exertion is often suggestive of a polyp. Small cervical polyps are, at times, too soft to be detected by palpation, but inspection through a bivalve speculum discloses them. The removal is usually simple, but the essential thing is a microscopic examination of the tissue. The incidence of malignancy is very low, but occasionally a malignant change may occur in a polyp or an endocervical epithelioma may peep through the external os, appearing not unlike an innocent polyp.

Occasionally, acquired stenosis of the cervix may be responsible for the appearance of blood in the vagina. After cauterization, stenosis at the external os may result when the proper precautions to prevent it are neglected. Menstrual blood accumulates in the uterine cavity. When the intra-uterine pressure reaches a point sufficiently high to overcome the resistance at the cervix there is a discharge of old brown blood

*Read in Joint Session, Section on Obstetrics and Section on Gynecology, Southern Medical Association, Thirty-Fourth Annual Meeting, Louisville, Kentucky, November 12-15, 1940.

which often continues to dribble forth intermenstrually. Occlusion of the cervical canal occasionally occurs spontaneously after the menopause. The endocervical and endometrial glands continue to secrete and the secretion often becomes infected, causing ulceration of the endometrium and some bleeding. The characteristic discharge which is expelled, often intermittently, is purulent with tinges of blood.

The diagnosis of typical advanced carcinoma of the cervix is all too familiar to all of you, but there are a few points which I want to emphasize. One of them is that a cervix which feels normal and appears normal through the speculum may harbor an endocervical carcinoma and even a rather advanced lesion which can only be diagnosed by curettage of the endocervical canal. The second point which I wish to emphasize is that all suspicious lesions should be biopsied. By suspicious lesions I refer to small granular looking areas, which bleed when rubbed with a cotton applicator, whitish areas suggesting leukoplakia, abnormally hard areas and areas raised above the surrounding level suggesting cellular proliferation. Spraying or painting the cervix with Lugol's or Gram's iodine solution as described by Schiller often aids in localizing the area to be biopsied. The third point which I wish to emphasize is the importance of having biopsied tissue examined by a competent gynecologic pathologist. Specimens which have come to my attention within the past few years have convinced me that many uteri are removed or treated by radium for cancer when cancer does not actually exist. There are lesions in the cervix which are cancer-like in their histologic appearance which have no relation to true cancer. Most of these are due to metaplasia of the columnar epithelial cells of the endocervix and glands, forming squamous-like plaques of cells which are often at some depth beneath the surface of the cervix. Our conviction that these lesions have no relation to cancer is based upon follow-up studies of many patients having such lesions. Many pathologists, being somewhat uncertain of the nature of these lesions, hide behind the term "precancerous." This results in the removal of many uteri unnecessarily and, although this is not so grave an error as to permit an existing cancer to remain untreated, it is still serious and should be avoided. Better training in gynecologic pathology on the part of gynecologists and general pathologists is the only remedy.

The mechanism by which myomata give rise to hemorrhage is not always obvious. Often even when the myomata are of considerable size their presence may not be responsible for the bleeding which may be functional and the myomata only incidental. Another point worthy of emphasis is that a small submucous fibroid may give rise to profuse hemorrhage and yet not be recognizable on bimanual examination. In all cases in which curettage is done to determine the cause of bleeding, such a possibility must be considered and the cavity explored for irregularities which might be caused by such a tumor. Another point concerning fibroids worthy of discussion is their relation to postmenopausal bleeding. If a bleeding woman presents herself for examination after the menopause and examination reveals the presence of a fibroid, is one safe in assuming that a benign fibroid is responsible for the flow? The answer is in the negative. The fibroid may cause the bleeding, for it is apparently possible for a fibroid which was intramural and asymptomatic before the menopause to work itself into a submucous position after the menopause and cause bleeding. The basis for this statement is the study in our laboratory of uteri removed for bleeding after the menopause from women in whom there was no previous history of profuse periods which would have certainly occurred had the tumors occupied that position before the end of the woman's menstrual life. Often, however, a fibroid which is responsible for bleeding after the menopause has undergone sarcomatous change. But still more frequently, bleeding from a myomatous uterus after the menopause is due to some other lesion occurring with the fibroid and in many instances this lesion is malignant.

The endometrial polyp is a lesion which may cause slight or profuse bleeding and the presence of which is often not detected. The bimanual examination being negative, a diagnostic curettage is done. The polyp may easily be missed with a curette and when removed is usually minced up with the rest of the curettings and unrecognizable. It is my belief that many cases of "functional bleeding" which are cured by a single curettage are explained on the basis of an unrecognized endometrial polyp.

Carcinoma of the corpus uteri is a disease of the menopausal years and beyond. We have seen endometrial carcinoma in a girl of 22, but such instances are extremely rare and for practical purposes one scarcely need consider this lesion until after 40. The importance of its early recognition is emphasized by the fact that when diagnosed even reasonably early there is an excel-

lent chance of cure by a combination of intrauterine radium, x-ray and panhysterectomy.

Carcinoma of the tube may make itself manifest by a blood-tinged discharge, but this is an extremely rare lesion. Of more practical value is the fact that in salpingitis there is often an associated uterine bleeding. In the acute stage of the disease, when the gonococcus is en route from the cervix to the tube via the endometrium, there is a transient endometritis often with small areas of ulceration and consequent bleeding. Later in the course of the disease, when the diseased tubes lie in proximity to the ovaries, the latter organs are often involved in the inflammatory process and their function disturbed. This often results in too frequent or too profuse menstruation or, at times, intermenstrual bleeding. Here, then, is an example of functional bleeding of the uterus, dependent upon organic disease in the adnexa. In ectopic pregnancy we have another example of a certain type of functional bleeding of the uterus dependent upon an organic lesion in the tube. In certain cases the hemorrhage into the tubes, especially when the pregnancy lies near the cornual end of the tube or in the cornu of the uterus, may flow into the uterine cavity and thence into the vagina. But this is not the usual mechanism of the vaginal bleeding seen with ectopic pregnancy. In most cases the placenta separates from the tubal wall and the embryonal sac is cast off into the lumen of the tube or into the abdominal cavity. The fetus dies and the corpus luteum degenerates. Progesterone is withdrawn from the circulation and the decidua, which is dependent upon the progesterone for its existence, is cast off and bleeding results. This bleeding is usually no more profuse than a menstrual period, but is apt to persist as a slight show for days after the more profuse initial flow. Indeed, physiologically, this form of bleeding actually represents a delayed menstruation.

The role of ovarian neoplasms in uterine hemorrhage is an important one, for bleeding may be the first sign which the patient has that anything is amiss. This is not to say that all ovarian tumors cause uterine bleeding, for this is not the case either before or after the menopause. Before the menopause the majority of ovarian growths cause no change in menstruation, but a certain number may cause a disturbance of the cycle varying from amenorrhea to menorrhagia or metrorrhagia. Much has been written about granulosal cell tumors and their endocrine action causing uterine bleeding and particularly postmenopausal bleeding. But it is erroneous to assume that only this type of tumor can be responsible for bleeding after the menopause. One-fourth of all of our ovarian tumors occurring after the menopause were found to be associated with bleeding, and among these practically all of the usual histologic types, both benign and malignant, were represented. The explanation for the bleeding is not always apparent. In some of the malignant tumors extension of the neoplasm to the endometrium was the cause of the bleeding, but in many the explanation is not clear and we must be content with assuming some form of ovarian dysfunction.

After this short resume of the commoner organic lesions which may be responsible for bleeding, it is obvious that it is never safe to assume bleeding is functional without the necessary examinations to exclude these lesions. In the practice of gynecology one finds all too often that practitioners do exactly this. I have found practically all of these lesions in bleeding women who had been treated on the assumption that they were functionable bleeders. The delay in instituting the proper therapy when malignancy is present may mean death to a patient who could have been saved had a correct diagnosis been made earlier. Unfortunately the many hormones now on the market which are sold by high pressure salesmen give the indolent practitioner a method of treating bleeding women which he seizes upon, often omitting a careful bimanual examination, cervical inspection, cervical biopsy or endometrial curettage.

Discussion follows paper of Dr. Novak, page 416.

ENDOCRINOPATHIC UTERINE BLEEDING*

By EMIL NOVAK, M.D.
Baltimore, Maryland

Few subjects in gynecology have been so intensively studied and so widely discussed in recent years as that of functional uterine bleeding. There is no reason to believe that the disorder is any more common than it has always been, and the reason for its present prominence in the

*Read in Joint Session, Section on Gynecology and Section on Obstetrics, Southern Medical Association, Thirty-Fourth Annual Meeting, Louisville, Kentucky, November 12-15, 1940.

*From the Department of Gynecology, Johns Hopkins Medical School.

literature lies in our growing knowledge of the normal and pathologic physiology of the reproductive cycle. This new knowledge has thrown much light upon all the disorders of menstruation, including functional excess. This is implied by the very designation of "functional" to a form of bleeding once spoken of by the meaningless term "idiopathic." The literature of an earlier day is full of papers explaining this disorder as due to vascular lesions, such as arteriosclerosis and excess of elastic tissue, and to lesions of the uterine musculature, such as myometritis, fibrosis, or the "insufficientia uteri" of Theilhaber.

The first vague intimation that abnormal bleeding might be due to functional rather than structural factors came in the suggestion of Brennecke, as far back as 1882, that the endometrial lesion now designated as hyperplasia is the result of endometrial hyperemia produced by abnormal ovarian stimuli which involve the nerve mechanism formerly accepted as explaining menstruation. The term "endometritis ovarialis" was given by Brennecke to the characteristic endometrial pattern now called hyperplasia, and its association with uterine bleeding was recognized. And this was many years before anyone had thought of the ovary as an internal secretory gland, and, indeed, fully 25 years before the term hormone had been coined.

The credit for establishing hyperplasia of the endometrium as a distinct and non-inflammatory entity belongs to Cullen and Schröder, and to the latter must go the credit of first establishing, by histologic studies, that the causative ovarian disturbance consists in an absence of active corpora lutea and an abnormal persistence of the functioning follicle. This important contribution, made long before the isolation of either of the two ovarian hormones, was the starting point in the more direct studies of the problem which later advances in endocrinology have made possible.

As a matter of fact, investigators for many years have concentrated their study of functional bleeding almost solely upon the endocrine factors involved. This is not surprising if we stop to think that pretty much all that we have learned as to the physiology of menstruation revolves about its endocrinology. And yet other factors must be important, such as the role of the vasomotor nerves, that of the uterine muscle, and that of the uterine blood vessels. With reference to the latter, our knowledge has been greatly increased in recent years, as I shall presently discuss. This multiplicity of cogs in the menstrual mechanism is emphasized because any one or more of them may be involved in functional bleeding, so that not all cases of the latter are to be explained, as we were wont to do formerly, by the simple common formula of excess of estrogenic hormone and lack of progesterone. Numerous cases are now recognized which do not conform to this pattern, and which are nevertheless properly classed as functional.

Unfortunately, we know practically nothing as to the role of the vasomotor nerves in either normal menstruation or abnormal bleeding, and almost nothing as to the role of the musculature, significant though it may well be if we recall how important the muscularis is in the regulation of obstetrical hemorrhages. As for the blood vessels themselves, a contribution of the greatest importance has been made by Markee in his demonstration of the fundamental role played in normal menstrual hemorrhage by the spiral arterioles of the endometrium. By direct study of endometrial tissue implanted into the anterior chamber of the eye of the experimental animal, he has clearly established that alternating spasm and dilatation of these vessels brings about the blushing-blanching phenomenon, and that menstrual bleeding is the composite result of small isolated non-synchronized hemorrhages from individual spiral vessels as a result of the ischemia produced by prolonged spasm.

These studies emphasize that menstruation is dominantly a vascular phenomenon, but this concept is not at all incompatible with acceptance of the fundamental role of endocrine factors. Nothing can be more certain than that these vascular phenomenon are under the control of the ovarian hormones, but we are still ignorant of the nature of the link-up between the endocrines and the vascular apparatus.

MECHANISM

As already mentioned, the starting point in efforts to explain the mechanism of functional bleeding was the work of Schröder in 1915. By correlated histologic studies of the uterus and ovaries in such cases he concluded that the bleeding disorder to which he gave the name of metropathia hemorrhagica is produced by abnormal persistence of unruptured follicles, with consequent absence of functioning corpora lutea, and with the production of hyperplasia of the endometrium as a result of the abnormally persistent and excessive estrogenic stimulation. This is still the accepted explanation for perhaps

the largest number of cases of functional bleeding, and for this viewpoint there is much evidence, such as the experimental production of hyperplasia in castrated animals and also in castrated human females.

Since then, however, we have learned that not all cases of functional bleeding are to be fitted into one mould. In many, for example, the endometrium is not hyperplastic, and it may actually be atrophic. Moreover, in a not inconsiderable proportion of cases, the endometrium may actually be of progestational rather than proliferative type, indicating that the cycle is of ovulatory and not anovulatory character. We are still in the dark as regards the mechanism of the bleeding in cases of the former variety. A possible explanation is a quantitative imbalance between the two ovarian hormones, but perhaps dysfunction of the uterine musculature, disturbances of the vasomotor nerves, or disorders of the spiral arteriolar system may prove to be more important. It seems useless to speculate further about this group in the present state of our knowledge.

The fact remains that a large, and in my opinion the largest, group is to be explained by a failure of ovulation, with abnormally persistent estrogen output, and with absence of corpora lutea and progesterone, in line with Schröder's original theory. No one can afford to be arbitrary in this explanation, but it is, as already mentioned, supported by considerable evidence. Such a mechanism represents simply an exaggeration of that seen in the anovulatory type of menstrual cycle, the not infrequent occurrence of which is now generally accepted.

Even granting the correctness of the above explanation as to the underlying ovarian dysfunction, there remains the still unsolved question as to how this brings about endometrial bleeding. It seems probable, and I myself have held the view, that the bleeding phases are brought about by temporary drops in the estrogen level because of the inhibition of pituitary gonadotropic function which is produced by more than a certain level of estrogen, quantitatively different in different women. This is a very general statement, and it blankets certain other individual imponderables such as the receptivity or refractoriness of individual endometria to the ovarian hormones, of certain ovaries to the pituitary gonadotropes, and of individual hypophyses to the ovarian hormones.

Our ignorance on these points is not surprising, for we know very little as yet concerning the bleeding mechanism of normal menstruation. This is not the place to review the physiology of the normal cycle, but one or two points may be alluded to, because they are pertinent to our present subject. First, there is now almost universal acceptance of the concept that the immediate factor in functional endometrial bleeding, normal or pathological, is a withdrawal or abrupt diminution in the ovarian hormones. This hormone deprivation theory explains such bleeding adequately, without the necessity of invoking a positive bleeding factor. The latter concept was suggested some years ago by Hartman and his collaborators, but later abandoned by them. More recently it was revived by Kurzrok, but the evidence for such a positive factor is extremely unconvincing. When the endometrium is built up under the influence of estrogen alone, or of estrogen supplemented by progesterone, in either case withdrawal of the hormones is followed by bleeding. In most cases of functional bleeding estrogen withdrawal alone is concerned. On the other hand, in the bleeding of normal menstruation, the evidence indicates that the withdrawal of the progesterone is the important factor.

An extremely interesting observation has recently been reported by Zondek, who found that five successive daily injections of 10 mg. of progesterone, when given just after menstruation in the follicular phase of the cycle, would bring about uterine bleeding within 72 hours. No explanation of this phenomenon was given by Zondek, nor does one seem possible in the present state of our knowledge. However, the fact that a certain amount of estrogen must be present in order to produce the bleeding effect of the progesterone points strongly, as do certain other endocrine phenomena, to the importance of an interaction or imbalance between the two hormones in the production of abnormal effects.

The second point I should like to emphasize is that the histology of the endometrium, important as it is, is not an infallible index of all the functional effects of the ovarian hormones. Let me illustrate what I mean by an example furnished by another recently published study by Zondek. The finding of a typical secretory endometrium by biopsy just before or preferably on the first day of menstrual bleeding is accepted by all but a few dissenters as a reliable indication that ovulation has occurred. But such secretory endometria may differ in the character and degree of their secretory activity, ordinarily manifested by production of mucin and glyco-

gen. Zondek has shown that in some cases the secretion consists dominantly of mucin, with marked deficiency of the glycogen essential to the implantation of the fertilized egg (glycopenia of the endometrium). In other words, a histologically typical secretory endometrium may be inadequate for implantation purposes.

A more pertinent example is to be seen in the frequent disparity between the growth and bleeding effects of the estrogenic hormone upon the endometrium. Functional bleeding can occur not only from an endometrium in which hyperplasia has been brought about by excessive estrogenic stimulation, but also from endometria in which little or no growth effect is evident, endometria which correspond perhaps to an early interval phase or which may even be atrophic. One of two explanations would seem to apply to such cases. It is probable that certain endometria are refractory to the growth effects of estrogen, although the interplay between ovarian and pituitary sex hormones still goes on, with periodic drops in the relative estrogenic levels, and with therefore attacks of uterine bleeding. Or the bleeding spell takes place at such low estrogen levels that a growth effect in the endometrium is not produced. Hormone studies of the urine have not yet clarified this problem for us.

My paper would no doubt make much more pleasant reading if I could give a simple and stereotyped explanation of the mechanism of functional uterine bleeding in general, but I have chosen rather to discuss some of the many still-existing gaps in our knowledge, as they go far to extenuate the still unsatisfactory status of our therapy of this disorder.

CLINICAL CHARACTERISTICS

The clinical characteristics of endocrinopathic functional bleeding scarcely need elaboration. The disorder may occur at any stage of reproductive life, but more than half of all cases, in my own experience, have been observed during the fifth decade. A considerable number, probably about 10 per cent, occur in the pubertal and early adolescent years. The bleeding is perhaps more characteristically of the menorrhagic type, but metrorrhagia is also very common. Continuous uterine bleeding sometimes appears to be due to the fact that each menstrual period is so prolonged that it extends into the next period. The bleeding may be alarming in amount and a number of fatal cases have been reported, though I have not personally observed any instance of this sort in an experience with many hundreds of cases. Pain is characteristically absent, but sterility is the usual rule. Many patients, however, have previously borne children or do so after readjustment of the hormone mechanism. The obvious explanation of the sterility is the fact that ovulation is lacking in most cases of this type.

TREATMENT

The treatment of this disorder is influenced by two chief factors, the age of the patient and the importance or unimportance of preserving the reproductive function.

First of all, it should be remembered that no sharp dividing line can be drawn between the quantitatively normal menstrual periods not infrequently associated with the anovulatory mechanism and the pathologically excessive bleeding in which the same underlying mechanism is concerned. Just as the girl at puberty often exhibits anovulatory cycles which by spontaneous readjustment of the hormone mechanism become ovulatory in character, so may similar spontaneous readjustment of the mechanism bring about spontaneous cure of functional bleeding. This is particularly true of the milder forms of bleeding so often seen in the pubertal and premenopausal periods of life. A considerable proportion of girls exhibit not only marked irregularity, but also moderate excess of menstruation for periods of from several months to several years after initiation of the function. And many of these then, without treatment, fall into a normal menstrual swing. A similar observation may be made in women approaching the menopause, a certain proportion of whom unquestionably cease ovulating a considerable time before they cease menstruating. Such anovulatory cycles may be moderately excessive. While we very properly teach women that flooding at this time is never to be looked upon as normal, the fact remains that many women who disregard this teaching cease bleeding spontaneously, through final cessation of ovarian function.

When, however, the abnormal bleeding becomes very free or alarming, the patient is quite sure to seek advice. If she is in the menopausal group, the treatment is simple and highly satisfactory. At this age the first essential is to make sure that the bleeding is really functional, and that no structural lesion, such as uterine or ovarian neoplasm, is present. If pelvic examination reveals no evidence of this, the next step is to eliminate intra-uterine pathology and es-

pecially adenocarcinoma of the uterus. This can be done only by diagnostic curettage and microscopic examination. If the latter reveals an endometrium of proliferative or hyperplastic type, or even one corresponding to any of the normal menstrual phases, it is fair to conclude that the bleeding is of functional origin.

Once this has been settled, the further management is clear. Women at this phase are rarely anxious for further pregnancies, and practically 100 per cent of such cases can be cured by abolishing ovarian function by radiotherapy. This is not the place to discuss the technic of the latter procedure, but an effort should be made to give sufficient dosage to abolish ovarian function completely. Some ovaries are notoriously hard to kill, and after insufficient dosage bleeding may reassert itself in from a few months to several years. This may be disconcerting, because while such bleeding is very likely to be again of functional nature, it is difficult, without repetition of diagnostic curettage, to eliminate an intercurrent intra-uterine carcinoma. All in all, however, the treatment of functional menopausal bleeding represents one of the most satisfactory applications of radiotherapy in the field of gynecology. There is rarely any justification for hysterectomy unless there is some other indication for opening the abdomen, in which case there can be no objection to simple removal of the uterus.

The problem is far more difficult and unsatisfactory in younger patients, in whom the matter of future reproductiveness is usually of the greatest importance, not to speak of the importance of preserving ovarian endocrine function. In the case of very young patients curettage is not usually necessary for diagnostic purposes, and if simple pelvic examination reveals the essential normality of the pelvic organs, there is little risk in assuming that the bleeding is of functional nature. Occasionally curettage is necessary for its immediate therapeutic effect, for it rarely fails to check the bleeding temporarily. It need hardly be added that the operation should be preceded by transfusion if the bleeding has been at all alarming.

It is in this group of younger patients, in whom more radical and more certain measures are contraindicated, that we have our great field for such organotherapy as is now available. Radiologists agree with gynecologists that radiotherapy should, as far as possible, be avoided in patients of this group, even in carefully controlled doses designed to check the menstrual function only temporarily. In the occasional intractable case such regulated radiotherapy may be justified, though most gynecologists would probably prefer occasional repetition of curettage. Some ovaries are singularly sensitive to the effects of radium and x-ray, and I have personally observed a number of instances in which even small dosage in the hands of expert radiologists has been followed by permanent abolition of ovarian function. Moreover, there is still no unanimity as to the effect of such treatment upon future pregnancies, particularly with reference to the possibility of defective offspring.

From what has been said as to the incompleteness of our knowledge of the pathologic physiology of uterine bleeding, it is not surprising that the organotherapy is still far from satisfactory. It is based chiefly on the concept that the bleeding is due to relative excess of estrogen and lack of progesterone, and it aims chiefly to increase the progesterone, or to lessen and counteract the estrogen. The following organotherapeutic plans may be discussed in summarizing fashion:

(1) The use of pregnancy urine or chorionic hormones. The original employment of these substances was based on the hope that the pregnancy urine hormone principles might produce luteinization in the human ovary as they do in the ovaries of experimental animals, thus supplying the lacking hormones. It should be remembered that when this clinical experiment was made progesterone itself was not available for clinical use. Histologic studies of the ovaries of treated women soon established that the desired luteinization was not produced, but the fact remains that many clinicians have reported good results in a certain proportion of cases. On the other hand, no one can claim consistent or highly satisfactory results, nor has anyone been able to explain how such substances exert their effect. It has seemed to me that a larger proportion of cases respond to these pregnancy urine preparations than to progesterone itself, especially when the latter is used in small dosage. When these preparations are used, the usual plan is the hypodermic injection of doses of 200 to 500 units daily with the onset of bleeding, continued until bleeding is controlled or until six or eight injections are given. If free bleeding persists beyond this, not much is to be expected from further injections, and other plans of treatment should be resorted to.

(2) The use of progesterone. This hormone is now readily available commercially, though

still quite expensive in the dosage often indicated in the treatment of functional bleeding. Certainly no one would expect to bring about secretory changes in a proliferative type of endometrium with doses of from 1 to a few milligrams daily for a few days, and the many reports of good results with such dosage are better explainable by the assumption that the disordered bleeding mechanism is influenced by much lower dosage than is required to bring about histologic changes in the endometrium. This is in accord with what has been said in a previous paragraph as to the different thresholds of hormone sensitivity of the various endometrial functions.

(3) The use of testosterone propionate. The effect of the androgenic hormones upon the female cycle has been much studied during the past two or three years, and there is still much that is not clear. Almost all investigators believe that the effect upon the growing follicle is an inhibitory one, and that thereby estrogen production and endometrial proliferation are lessened. There is evidence, too, that in the progestational phase of the ovulatory cycle the effect of progesterone is supplemented and enhanced by the androgenic principle.

It is not surprising that the male sex hormone substance, in the form of testosterone propionate, has achieved much recent vogue in the treatment of functional bleeding. At the outset I may say that in my hands it has yielded more satisfactory results than either progesterone or the pregnancy urine preparations. During the bleeding phases it may be given intramuscularly in doses of 10 milligrams three times a week, and in the more severe cases 25 milligrams twice a week. Much larger doses are used by some, but I believe that this tendency should be avoided. A number of reports have been published of hirsutism and occasionally other masculinization phenomena such as change in voice. Such symptoms apparently disappear with withdrawal of the drug, though very slowly.

In any event such sequelae are highly undesirable, and if they were at all common most of us would no doubt feel that the use of testosterone would scarcely be justified. I do not believe that the use of the moderate dosage I have suggested is attended with any worth-while risk of such unpleasant symptoms, especially if it is avoided in patients who already show a tendency to hirsutism or excessive pigmentation. My own policy is to avoid the larger doses, and I have never given more than 50 milligrams a week, especially when, as in cases of functional menorrhagia, the hormone is kept up throughout the cycle. It behooves all of us, in these early days of testosterone therapy, to be constantly on the alert for undesirable by-effects, such as those I have mentioned, until further experience enables us to evaluate more intelligently the safety or the hazard involved.

(4) The use of thyroid extract. In only the occasional case of functional bleeding does hypothyroidism appear to be a factor, but when it is, thyroid therapy is indicated and is likely to be curative. I have recently observed a striking case of this sort. The patient was a woman of 32 who had for several years before I saw her been taking huge doses, 20 grains a day, of thyroid extract, with no evidence of saturation symptoms, and with a basal metabolic rate still slightly on the minus side. If this dosage was stopped or markedly lessened profuse menorrhagia would always appear, with return to a normal menstrual amount with resumption of the thyroid. In the overwhelming majority of cases of functional bleeding, however, no thyroid element appears to be concerned, and thyroid therapy is of no value.

(5) Other measures. Hamblen has recently reported good results in functional bleeding from what he speaks of as the cyclic employment of estrogens and progesterone, or of progesterone alone. No other reports on this method have as yet appeared, and it seems too new to permit of evaluation. Pregnant mare serum preparations have likewise been tried, but in my own small series of cases have produced no noticeable effect. It need hardly be stressed that general building-up measures are never to be overlooked, and that hematinic treatment, and not infrequently transfusion, are often called for. I have in previous papers mentioned the desirability, in the occasional cases in which this is practicable, of using for transfusion the blood of pregnant women.

SUMMARY

The logical point of departure in the study of functional bleeding is the study of the mechanism of normal menstrual bleeding, in both the ovulatory and anovulatory types of cycle. There are still many gaps in our knowledge, and some of these are discussed in this paper. Abnormal bleeding may occur from practically any type of endometrium, and the mechanism is certainly not the same in all. A large proportion, however, fall into the group characterized by absence of ovulation, with a relative excess of estrogen

and an absence of progesterone. The management of functional bleeding has been discussed, with particular reference to its organotherapy.

DISCUSSION (*Abstract*)

Symposium on Uterine Bleeding, Papers of Dr. Eastman, Dr. TeLinde and Dr. Novak.

Dr. F. M. Massie, Lexington, Ky.—My position in the discussion of this symposium is to present the attitude of the general surgeon whose major interest is gynecology.

Dr. TeLinde mentioned office biopsy. Biopsies done in the office to study uterine endometrium in seeking the cause of functional bleeding are not only permissible but desirable. In the older age group I think office biopsies are to be condemned. If the condition is not clearly functional, in our experience much the safer thing to do is to have the patient not only prepared physically but prepared mentally for a much larger procedure if this is necessary, even if the lesion seems to be on the surface quite benign. This attitude has borne fruit in a patient whom I have seen recently, 65 years of age with a perfectly benign looking and quite benign cervical polyp. Because I did not remove it in the office, I discovered quite coincidentally an adenocarcinoma of the fundus.

Another point which I wish to emphasize is one of which we are all quite aware. Patients in the fifth decade, from 40 to 50, with the so-called functional premenopausal bleeding should have more than a simple bimanual office examination. We are likely to turn these patients over for irradiation without further observation. It seems to me reprehensible that patients in this particular age group, from 40 to 50, who have not yet reached the menopause but whose bleeding is quite irregular and profuse, often do not have the advantage of a thorough diagnostic curettement in the hospital with the stage set for whatever major or minor procedure is necessary after that point. Whether it is intrauterine irradiation, which I prefer in this group of cases in the absence of organic lesion, or whether it is x-ray therapy after they leave the hospital, I do not think those in the 40 to 50 age group ought to be subjected to deep x-ray therapy without diagnostic curettement.

The other point I wish Dr. Novak would discuss when he closes, because he has some very definite ideas on the subject, is thyroid therapy in irregular profuse bleeding, particularly in younger women. Many physicians who have seen these patients have felt that it was justifiable, even in the absence of a basal rate, to use the therapeutic test of small doses of thyroid. Patients who have certainly not had hypothyroidism and who do have functional bleeding, who have been improved by the use of thyroid, fall into the large group, which Dr. Novak has mentioned, who would have established their own normal cycles without help or hindrance from us.

Dr. J. W. Kelso, Oklahoma City, Okla.—Some of us in Oklahoma take issue against urgent treatment of ectopic pregnancy, and we have set down the dictum that a woman whose ectopic pregnancy ruptures in the country will never die of the ruptured ectopic pregnancy, but if it ruptures in the city where the surgeon stands with his scalpel in his hand, she will die from the operation and not from the ectopic pregnancy. These women are in extreme shock, not from the hemorrhage alone, but from the peritoneal insult as well, and should be handled like any other patient who is in shock, and I am sure that you would not operate upon her abdominally.

We have had a rather contradictory paper today compared to one day before yesterday, when the essayist objected to the massage of a bleeding uterus. I agree with the essayist of today that massage of the uterus is a very able way to control postpartum bleeding.

Any woman past the menopause who begins to bleed has a carcinoma until proven otherwise, but the vaginal smear and the biopsy of the endometrium certainly will often lead to a diagnosis of a granulosa-cell tumor should this be present. These patients should all be thoroughly investigated, and too often they will be found to have organic lesions.

Functional bleeding as a term may belong in the same category as eczema to the dermatologist; it means that he does not know what is the matter with the patient. Too often functional bleeders turn out to be organic bleeders. It has been shown by Dr. Greenblatt and others that ovaries in women bleeding abnormally cannot be stimulated like a normal woman's ovaries. Therefore, these women are probably organic bleeders and not functional bleeders. We physicians as a whole are too often eager to accept the word of an author who is overenthusiastic about a problem that he is trying to solve and publishes enviable and unparalleled reports. Dr. Novak is very cautious in what he tells us to do and not to do, and the results he expects to receive from the treatments. Likewise we are overrun with expert representatives who come to our office with the answers to all our problems which we are unable to solve.

As to why some of these patients do or do not bleed, we might refer to some work that is being done at Houston, Texas, by Dr. Karl Karnaky. Dr. Karnaky has found that by giving huge doses of stilbestrol he can cause these women to stop bleeding, and with this he has conceived a new idea of why a woman menstruates. He believes that a woman must have an estrogenic level above which she does not menstruate and below which she does. This might explain Dr. Novak's case, in which he gave progesterone in big successive doses and in seventy-two hours the woman bled. The progesterone in some way neutralizes or counteracts the estrogenic substance, lowers the estrogenic level and, therefore, the woman bleeds. Also we are all familiar with the withdrawel of estrogenic substance from patients who have had goodly amounts of estrogenic substitution. It is not unusual for that woman to bleed. Possibly that will be explained by Dr. Karnaky's idea of the estrogenic level in the blood.

Testosterone will inhibit ovulation through its effect on the pituitary glands and this in turn will inhibit the development of progesterone, which in turn will not decrease the woman's estrogenic level of bleeding and, therefore, she does not bleed. We should be very reluctant to accept the recommendations for the use of these expensive drugs before their value has been definitely established.

Dr. Gilbert F. Douglas, Birmingham, Ala.—Has Dr. Novak had any experience with or does he give the pituitary substances in cases of bleeding at puberty

with anovulatory patients with the idea of stimulating ovulation?

Dr. Misch Casper, Louisville, Ky.—I should like to ask Dr. Novak two questions. One of them has been propounded recently, that is, whether he has had any experience with the fact that the estrogenic hormone acts through the pituitary rather than having an effect on the ovary.

In former discussions of this subject Dr. Novak has always held up thyroid extract as perhaps the most reliable of all the hormones that stimulate ovarian function. I should like to ask him if he has anything new and if there has been any change in the conception of the relation of the thyroid to these other hormones. Lately it seems to be that it is the pituitary that acts as a governor, as it were, regulating the other hormones. I should just like to know if as a result of his research he has something new to tell us about the relation of the thyroid to the other endocrine glands.

My experience with these hormones is that we are still in a stage of trial and error, and in no two cases will the symptoms work out just as we think they will for the indications as presented.

I should like to know whether any recent work on the cell count of the vaginal epithelium or secretions can help us practically in the diagnosis?

Dr. TeLinde (closing).—The practice, which is not uncommon, of practitioners who, finding no gross organic lesion to account for the bleeding, send the woman to an x-ray man for x-ray therapy, is pernicious. I have operated upon many such women later for carcinoma of the corpus uteri which should have been discovered months before.

I agree also with what Dr. Massie says about the use of the suction curette as an office procedure. I do not mean to belittle it. We use it a great deal, particularly to determine whether women are ovulating, but when I suspect a malignancy and do a curettage for ruling out malignancy, I much prefer to put the patient to sleep and to do a very thorough curettage.

There is another use for the suction curette which has not been emphasized, particularly in the literature, but for which we have found it very valuable. Women with functional bleeding often receive, as Dr. Novak has said, temporary benefit from curettage. Sometimes the benefit is of quite long duration, several months and even one or two years. Some of these women can be curetted time after time with the suction curette, a pretty thorough job be done and a great deal of benefit be had, tiding them over until the functional bleeding spontaneously ceases.

More endocrine knowledge or misinformation is disseminated to practitioners through the detail men than in any other manner. Dr. Kelso said one thing, however, with which I must disagree. I refer to his statement that ectopic pregnancies do not bleed to death and are sometimes killed by the additional shock of the operation. That is an old theory. Hunter Robb proposed it many years ago. I think there was an element of truth in it then. But that was before the days of transfusion. Today with transfusion available almost everywhere the problem has changed completely. Hunter Robb attempted to prove his theory in the experimental laboratory. He cut the ovarian artery and vein of a dog, but did not ligate them, and closed the abdomen. The dog showed no evidence of shock and ate his supper that night. Then Dr. Robb cut both ovarian arteries and veins and closed the abdomen without ligating the vessels. These dogs also showed no evidence of shock. Then he did a complete pelvic operation, taking out the tubes, ovaries and uterus, and tied none of the cardinal vessels. None of the dogs bled to death. He reasoned from that, if dogs do not bleed to death with the four cardinal vessels cut, why should a woman bleed to death from a branch of an ovarian vessel? But some of these women do bleed to death. I have seen women bleed to death from rupture of ectopic pregnancies while preparing for transfusion. I think that all Hunter Robb proved was that you cannot take everything from the experimental laboratory and apply it to clinical surgery.

Dr. Novak (closing).—Before answering the two or three questions which have been put to me I should like to reinforce what Dr. TeLinde has just said about the importance of treating cases of bleeding ruptured ectopic pregnancies as real surgical problems. As he says, anyone who has seen women die from this cause (and they can die) must feel that way about it. With the present day universal employment of transfusion, even those women who are shocked stand operation remarkably well and recuperate remarkably rapidly. The operation ordinarily requires very little anesthetic, and I have never seen a woman die from the effects of the operation since transfusion has been available. In examining specimens of ruptured interstitial pregnancy one may find the whole cornu of the uterus blasted out, and such women can die before operation is possible. Generally speaking, the risk to the patient is far less with immediate operation and transfusion than with delayed operation.

The importance of diagnostic curettage in women with menopausal bleeding has already been stressed. Until a comparatively few years ago it was a very prevalent practice for a physican to examine a woman with bleeding of this sort, to find nothing grossly wrong with the pelvic organs, and then to send her to the radiologist. This is a dangerous practice, and every gynecologist of experience has seen patients of this sort who later were shown to have some serious lesion, frequently carcinoma or submucous myoma. For the latter, as a matter of fact, radiologic treatment is ordinarily contraindicated. So a diagnostic curettage should always precede radiotherapy in menopausal treatment.

The question has been asked as to whether or not cases of functional bleeding occurring at the time of puberty can be treated by preparations which aim to promote ovulation. I am sure the questioner had in mind the new preparations of equine gonadotropic serum. These are the so-called pregnant mare serum preparations, available in a number of commercial forms. Pregnant mare serum preparations are designed for that purpose. They have been employed by veterinarians to increase the fecundity of droves of animals, but in the human being they still have to establish their value. Some of you have seen papers written by Davis and Robb and also Sigler. These preparations were highly lauded, but

the results have not been repeated by most other observers, and I think that they must be viewed very critically. A much more conservative paper has just been published by Irving and his associates. As yet there is no very effective way of making non-ovulating women ovulate, but ovulation is often established spontaneously, especially in the puberty type of bleeding.

Two questions have been asked with reference to the thyroid group of cases. There is no question that in a small group of cases the thyroid is the important factor. We have a certain definite but small group of functional cases of bleeding in which hypothyroidism is present, as determinable, for example, by general bodily manifestation of hypothyroidism and by basal metabolic tests. I have described in my paper a rather striking case of this sort. But in the usual type of functional bleeding no such relationship with the thyroid can be found.

Dr. Casper stated that in previous papers I have stressed the thyroid as perhaps the most important therapeutic agent in functional disorders, but this does not apply to functional bleeding. In the treatment of certain other functional disorders, as in some cases of sterility and amenorrhea, it is perhaps true that thyroid is more frequently helpful than any other endocrine substance, but that does not apply to functional uterine bleeding.

The question of estrogen level is nothing new. That has been the concept that everybody has had of these things. All women have certain quantitative hormone levels and there is, as an underlying mechanism of the menstrual cycle, a reciprocal relationship between the pituitary on the one hand and the ovary on the other hand, a sort of seesaw relationship. When the ovaries are inactive, or if they are removed, there occurs an excessive gonadotropic function of the pituitary. For example, we see in women at the time of menopause the disappearance of estrogen and a relative excess of the pituitary gonadotropes, which continues throughout the balance of the woman's life. If a woman with amenorrhea has a deficiently functioning ovary, one finds not only a deficient amount of estrogen, but also a comparative excess of the pituitary gonadotropes. On the other hand, if the ovary is excessive in its estrogenic function, the pituitary is depressed. As a matter of fact, the best hormonal means we have available clinically and therapeutically for inhibiting pituitary overfunction is by means of estrogenic therapy. We find application for this principle, for example, in the treatment of certain so-called pituitary dysfunctions in which the woman at the time of menstruation, and only at the time of menstruation, has violent headaches. The best treatment for that condition that I know of is to give large doses of estrogenic substance for some days before the beginning of menstruation. This inhibits the excessive pituitary activity, and frequently women who have these violent, strictly menstrual headaches for the first time in many years go through menstruation without any headache. That every woman does have an estrogen level has been recognized by physiologists for years, and it is perfectly true that we can inhibit the pituitary by means of estrogen, but that does not mean that we can always cure cases of bleeding by giving estrogen, as one might infer from the reports of Karnaky, which were mentioned by Dr. Kelso.

GASTRO-INTESTINAL ALLERGY*

ITS PRESENT STATUS

By ALBERT F. R. ANDRESEN, M.D., F.A.C.P.
Brooklyn, New York

Allergic reactions in the gastro-intestinal tract have been so common and so well-known to the average layman that it is surprising that the medical profession has been slow in recognizing allergy as an important cause of gastro-intestinal symptoms. Fifteen years ago, when I first wrote on this subject,[1] it was considered new, although I had been recognizing allergic gastro-intestinal reactions for twelve or fifteen years before that. Today we find some gastroenterologists who are still skeptical, others who consider gastro-intestinal allergy rare, and others who refuse to call it allergy, but speak of food sensitiveness or food idiosyncrasy. Although the literature on allergy in general is increasing each year by leaps and bounds, articles on its gastro-intestinal manifestations are still very rare. However, in recent years some very important work has been done in establishing the allergic reaction in the gastro-intestinal tract as a definite entity, and much has been accomplished in the diagnosis and treatment of this very distressing condition. The layman has long realized that "stomach upsets" have been caused by certain foods known to "disagree" with him. Many medical mistakes have been made by ignoring this observation on the part of the patient. When a patient declares that his heartburn, "gas," cramps, diarrhea or vomiting, his "bilious attacks" or "sick headaches," his acute abdominal pains or itchy anus invariably follow indulgence in certain foods and do not occur when these foods are avoided, his medical attendant should help him to prove or disprove the correctness of his observations, even though conducting a necessary search for organic causes for the symptoms.

FREQUENCY

The frequency with which allergic manifestations are the cause of gastro-intestinal symptoms may be judged from the high percentage of such cases occurring in a series of private patients who came to me for a gastro-intestinal survey. In a previously reported series of 3,412 private patients, 522, or 15 per cent, gave a history of al-

---

*Read in Section on Gastroenterology, Southern Medical Association, Thirty-Fourth Annual Meeting, Louisville, Kentucky, November 12-15, 1940.

*From the Gastro-intestinal Service of the Long Island College Hospital, Brooklyn, New York.

lergy in general, and 376, or 11 per cent, had definite gastro-intestinal manifestations. However, only 12 per cent of the allergic cases showed allergy alone, the remainder showing it only as a complication or perhaps a cause of organic disease, an important factor because it interfered with the use of the usual dietary measures in the treatment of the organic condition. The seriousness of the failure to recognize allergy is shown by the fact that 30 per cent of our patients had been subjected to multiple operations, many of them probably unnecessary. Appendectomy was the most common operation, having been performed in 21 per cent of the cases. A series of 49 patients had had 68 operations. The age of our patients varied from 7 years to 71 years, the average being in the neighborhood of 40 years. The sexes were nearly evenly divided.

CAUSE

Unfortunately the cause of allergy is not yet known, although its existence can be demonstrated and its hereditary transmission along Mendelian lines has been proven. The similarity between the mechanism of allergy and that of infection and immunity has long been recognized, although it is still a question whether the allergic reaction resembles the reaction of infection or that of immunity. An elaborate nomenclature has been developed by the allergists in order to facilitate the study and discussion of their problems, but this will probably need considerable revision when the chemical nature of allergy is finally determined. The fact that reactions exactly like those thought at first to be due only to unchanged proteins getting into the circulation can be caused by chemicals, drugs and even such physical agents as heat, cold and electricity, has complicated the picture, although the newer histamine theory presupposes that the causative agent, histamine, gets into the circulation as a result of the insult caused by the specific agent and is the cause of the reaction. Allergic reactions to bacterial proteins and to body secretions and hormones seem to occur, and the relation of endocrine disturbances, deficiency states and focal infections to the whole picture of allergy has been demonstrated. We are still far from an exact understanding of the mechanism of allergy. The clinician must now content himself with observing the phenomena known to be caused by specific agents to which an individual is sensitized and attempting to prevent or alleviate the symptoms. He must not neglect the patient because he does not know the exact chemical nature of the reactions he observes.

PROOF

The proof that allergic reactions occur in the gastro-intestinal tract is easily established. The fact that certain symptoms or physical signs occur invariably after the ingestion or inhalation of certain specific foods or other agents, disappear when these substances are eliminated and recur only when they are again taken, is certainly sufficient proof of the specificity of the reaction. Whether this phenomenon is called allergy, sensitiveness or idiosyncrasy makes no appreciable difference, as these three terms have not been shown to represent three entirely different conditions.

EXPERIMENTAL PROOF

Experimental proof of the specificity and nature of the allergic reaction in the gastro-intestinal tract has been amply demonstrated by Walzer, Gray, Harten and their associates.[2 3 4] Making use of the knowledge that tissues can be passively sensitized by the injection into them of the blood serum of persons known to be allergic to certain proteins, these investigators so sensitized the mucosa over hemorrhoids, in persons not otherwise subject to allergy, with serum from a person sensitive to peanut protein, and within five or six minutes after the subject had swallowed a peanut emulsion the mucosa over the hemorrhoid began to show pallor and excessive secretion. In motion pictures they demonstrated an increasing redness and secretion and a rapidly increasing edema, until the hemorrhoids had reached an alarming size before the reaction began to subside. Areas of skin sensitized at the same time showed urticarial wheals developing coincidently with the mucosal reaction. Subsequently the same group showed motion pictures of similar reactions occurring in the passively sensitized mucosa of the ileum and colon at the sites of ileostomies and colostomies. The reactions when the protein was taken by mouth always occurred almost as rapidly as when the protein was directly applied to the sensitized mucosa, proving the rapid absorption of unchanged protein after ingestion and the blood-borne nature of the reaction. Subsequently, in an effort to demonstrate the microscopic changes in the gastro-intestinal canal during an allergic reaction, the same workers passively sensitized the intestinal wall of rhesus monkeys at operation, observed the local reactions, and at their height performed biopsies, which showed the marked edema of mucosa and submucosa, the round-cell infiltration with eosinophils and beginning interstitial changes. Although they have

not yet shown them, it can readily be imagined what chronic changes would be produced by repeated or continuous reactions caused by the frequent ingestion of foods to which the gastro-intestinal tract is sensitized.

ALLERGIC REACTIONS

Observations of allergic reactions in the human gastro-intestinal tract are accumulating. Roentgenologists have observed the puckering of the mucosa of the stomach and duodenum or of the colon, with resultant motility disturbances, when the barium mixture contained substances to which the patient was sensitized. Kallos[5] has observed allergic reactions in the stomach, small and large intestines and gallbladder by gastroscopy, roentgen ray and at operation. Fries and Zizmor[6] have recently reported their clinical and radiologic observations following administration of known allergens to the barium mixtures given to children. Kaijser[7] resected a piece of human small intestine during an acute allergic reaction and found marked edema and eosinophilic infiltration. Appendices removed at operation for acute appendicitis often show similar allergic changes. We have frequently observed through the proctoscope the rapid clearing up of ulcerative lesions when certain foods were removed from the diet and their rapid recurrence when the foods were again ingested.

PATHOLOGIC CHANGES

The pathologic changes in allergy are quite definite, although, if the agent to which the gastro-intestinal tract or some part of it is sensitive is only occasionally absorbed, they may be quite transient in nature. As demonstrated by Walzer and others, the changes consist in hyperemia, edema and round-cell (usually eosinophil) infiltration of the deeper layers, especially the muscularis mucosae. Submucosal hemorrhages may produce petechiae or purpuric areas. If of short duration, the clearing up of these conditions leaves the organ normal. If frequent or continuous, such changes may be followed by local ischemia, necrosis and sloughing, with ulceration, hemorrhage or perforation. Repeated or continuous insults of this major type will result in chronic induration, fibrosis and adhesions. In the mouth, stomatitis, glossitis or only "canker sores" may occur. In the esophagus and stomach and duodenum, temporary acute episodes may occur or typical ulcers may develop, may produce complications and may require operation for them. In the intestinal tract, acute "food poisonings" may be a manifestation, or chronic changes with or without ulceration, perforation and sinus formation, such as regional enteritis or ulcerative colitis, may result. The well-known induration of skin and mucosa accompanying pruritus ani, or anal and rectal allergic ulcerations are also well known.

SYMPTOMS

The symptoms of gastro-intestinal allergy vary markedly with the nature and location of the lesion. In accessible and sensitive regions, like the mouth and anus, they consist of sensations or burning, pain, itching or bleeding. In the anus and in the rest of the gastro-intestinal tract the lesions manifest their presence by their effect upon gastro-intestinal motility and contractility or by the production of complications. The milder, temporary reactions may produce spasms at the cardiac, pyloric, ileocecal or anal sphincters, with resultant retrostaltic symptoms, such as fullness, belching, heartburn, sour eructation or regurgitation or even vomiting. Or, by causing irritation, they may produce hypermotility, with its resultant peristaltic unrest, cramps or diarrhea, or they may cause generalized colonic spasm, with constipation and the excessive secretion of mucus. Reactions in the biliary tract may cause typical gallbladder symptoms, often colic. At times, marked reactions in any of these locations may produce symptoms resembling an acute abdominal calamity or an acute intestinal obstruction, such cases, at operation, showing the typical allergic reaction often disappearing during manipulation, or showing no lesion at all, due to subsidence of the reaction during the preoperative period. Sloughing, ulceration and hemorrhage will cause marked hypermotility and active bleeding, with resultant anemia and prostration. With prolonged failure of absorption, signs of food deficiencies will become recognizable. With perforation, the characteristic agonizing pain may be present, followed by shock and the development of the symptoms of peritonitis, local or general. Where walled-off and not operated upon, subsequent infiltrations and adhesions may cause later angulations and obstructions, with their various, often confusing symptoms. Fibrosis with its stiffening effect, or cicatricial contractions with narrowing of the lumen, may also produce grave motility disturbances or obstructions. In addition to these varied symptoms which can be caused by allergy alone, the frequently coexistent organic diseases, not only gastro-intestinal, but respiratory, cardiovascular, renal or pelvic, may further confuse the picture, and under the

smoke screen of allergic symptoms those due to neoplasms may be unnoticed until too late for successful treatment. Neuropsychiatric conditions, frequently present, and often causing or caused by chronic diseases of any kind, may exaggerate or distort all of the symptoms, and require careful analysis.

DIAGNOSIS

The diagnosis of gastro-intestinal allergy is not so easy as many of the articles on this subject would seem to imply. It does not consist merely in the performance of some skin tests or the use of an elimination diet. It should not be considered the principal cause of a symptom-complex until a very complete study has been conducted, the principal features of which should be as follows:

(1) *History.*—A careful history should be taken, not merely the necessary history of any allergic manifestations in the family or in the patient's past life, but a complete general medical history covering all tracts and endeavoring to locate symptoms of non-allergic conditions. The family history is important, as allergy is known to be hereditary, although its manifestations may differ in different members of a family. A father with hay fever and a mother with migraine may have children exhibiting asthma, urticaria or periodic diarrheas. The same patient may show successively or coincidentally manifestations of allergy in several different locations, and the onset or cessation of allergic symptoms may occur at one of the periods of endocrine imbalance, such as puberty, menstruation, pregnancy, the menopause or in periods of marked emotional stress. The occurrence of bizarre symptoms, of symptoms not easily explainable on an organic basis or the cause of whose appearance or disappearance appears obscure, should engender a suspicion of allergy. Symptoms occurring at certain occasions, on certain days of the week, after eating in strange places, may often be explainable on an allergic basis. Symptoms of acute food poisoning occurring in only one person of a group who ate identical food are also suspicious. Often the patient's knowledge that certain foods in larger quantity always cause heartburn, vomiting, diarrhea, migraine or other allergic symptoms may suggest that smaller quantities of these foods, perhaps unknowingly ingested in food mixtures such as puddings, salads, soups or dressings may be causing chronic, more or less definite, symptoms. Drugs known to cause symptoms may also be taken in medicines not suspected of containing them.

(2) *Gastro-Intestinal Study.*—A complete gastro-intestinal study is imperative. Organic diseases of the gastro-intestinal tract may occur independently, organic changes may have been produced by the allergic reactions, or malignancy of the gastro-intestinal tract may be present. Failure to recognize any of these conditions is a serious matter.

(a) *Physical Examination.*—Physical examination may reveal nothing at all or may show allergic reactions present in skin, mucous membranes, eyes, chest or anus. Abdominal examination may show nothing abnormal, may reveal colonic spasm or may exhibit all the signs of an acute inflammatory or perforative lesion or an acute intestinal obstruction. Following a dose of epinephrine or ephedrine intramuscularly or sublingually administered, the sudden disappearance of these symptoms may give dramatic evidence of the allergic nature of the phenomenon. Esophagoscopy, gastroscopy and proctoscopy may reveal the allergic reactions before described. Physical evidence of deficiency states should be searched for.

(b) *Laboratory Examination.* — Laboratory examinations may be of much or little value. Gastric anacidity is supposed to facilitate absorption of unchanged protein, but is not often found to be present. Excessive secretion of gastric mucus is merely evidence of gastric irritation, which, when excessive, may also be accompanied by surface bleeding or ulceration, resulting in the finding of blood. Gastric analysis may also reveal hypermotility, or delay in emptying due to pylorospasm. Stools may contain excessive mucus, and in severe cases, as of ulcerative colitis, blood, mucus and even pus may be found in the diarrheal stools, together with a variety of bacteria, often erroneously considered to be the cause of the lesions found. Eosinophils in the rectal discharges are very suggestive of allergy, as is an eosinophilia, especially when protozoal infestation can be definitely ruled out. Evidence of deficiency states can be determined by laboratory tests. Blood calcium may be low and the sodium-potassium balance may be disturbed. It is important to make sure that blood coagulating factors are normal.

(c) *Roentgen Study.*—The roentgen study is of importance. Aside from determining the presence or absence of the various complicating organic lesions previously mentioned, a careful fluoroscopic and radiographic gastro-intestinal study, following barium meals and opaque ene-

mas, including mucosal studies, "spot films" and double contrast technics, will often reveal indisputable evidences of mucosal changes, as evidenced in esophagus, stomach and small intestine by puckering, coarsening or obliteration of mucosal workings or by evidences of ulceration or narrowing, and in the colon by smoothness, fuzziness, areas of defect due to ulceration of irregularities due to polypoid changes. Motility disturbances such as the various spasms, "writhing duodenum," "unstable colon" and haustral obliterations may be readily seen, and the complications, such as subdiaphragmatic air pockets in acute perforation, pockets or sinuses resulting from old perforations, or angulations and stenoses, cicatrices and adhesions are fairly easily demonstrable. Roentgen examination is also useful in observing the effects of administration and withdrawal of the offending factor. It must be realized that the barium suspension used may contain flavoring or other substances to which the patient is sensitized and thus be a cause of the reactions noted. In suspected allergic cases, only water suspensions of barium sulphate or bismuth subcarbonate should be used.

(3) *Specific Allergic Factor.*—The finding of the specific allergic factor or factors causing the allergic reactions is of course of the utmost importance, and is often very difficult, especially where different factors are responsible for various manifestations. These factors, as previously mentioned, may consist of drugs, chemicals, bacterial proteins, body hormones and other secretions, but in most cases foods are the principal offenders and a careful study of food factors constitutes the most important part of the study. In this connection it is of help to remember certain basic principles:

(a) *History.*—The history will often suggest the cause, as in the case of menstrual migraine, where some hormonal factor produced at menstrual period may be implicated, of an allergic reaction during activity at an infective focus, in which bacterial allergy may be suspected or of an attack following a new medication, when drug or chemical allergy would be the probable cause.

(b) The food causing a reaction may at times be suspected from the history, as in the case of patients who have taken a glass of milk as a cathartic, but have not suspected that small daily quantities of milk in coffee or cereal might be the cause of chronic diarrhea. It is self-evident that symptoms occurring at intervals must be due to foods taken only at such intervals, and that symptoms which are continuous, severe and chronic must be due to foods taken daily or very frequently. Attacks lasting only one or two days must be due to a single ingestion of the food, those lasting several days may be due to taking the leftover food on successive days in various forms, ending often in a soup. Attacks occurring at long intervals or at certain seasons make one suspect unusual foods or those ripening at the given seasons. Attacks occurring more frequently may be due to certain meats, fish, vegetables or fruits taken frequently, but not daily. Foods causing continuous, severe symptoms, obviously taken almost if not quite daily, would of necessity include such common foods as milk, egg, wheat, potato, orange and tomato.

(c) Sensitivity is constant and qualitative. Even a very small quantity of an allergen will give a reaction whenever taken, so that failure to show a reaction after ingestion of a suspected food rules out that food as a factor in the problem.

(d) Reactions may be enhanced by simultaneous ingestion of two or more foods to which a patient is sensitized or, at times when a solvent, like alcohol, is taken with the food, causing more rapid absorption.

METHODS OF DETERMINING THE ALLERGIC FACTOR

Various methods of determining the allergic factor have been suggested when the history alone fails to settle the question. Skin sensitization tests, of such value in hay fever and at times in other allergic conditions, have proven to be of little value in gastro-intestinal food allergy. Foods producing skin reactions by the scratch, intradermic or patch methods may or may not be concerned with gastro-intestinal symptoms and very often those proven to cause such symptoms will fail to give a skin reaction. Realizing that skin tests must be checked by actual feeding experiments, we long ago abandoned them as a routine procedure. Passive transfer may be of use in small children or very debilitated patients, but we have not resorted to it. The occurrence of a leukopenia following ingestion of a suspected food, the "leukopenic index," was much heralded when first suggested, but has now been pretty generally given up. It is now generally admitted that the actual experimental study of the effects of foods ingested is the most reliable method of determining the foods to which a patient is sensitized. Such a study was first attempted by Duncan Bulkey with his rice and water diet, three days of which he found

would clear up many previously stubborn skin lesions. By subsequent gradual additions of foods he demonstrated specific "idiosyncrasy" to certain foods which were shown to produce the skin lesions. Later, diaries kept by patients and showing all foods taken and all symptoms complained of, were carefully studied and often revealed such specific sensitivities. Then came the elimination diets of Vaughan, in which he demonstrated that frequently patients would react to several or all members of related groups of fruits and vegetables. Rowe and others have since devised other elimination diets, the principle of all of which involves the patient's exact compliance with sometimes rather complicated diet schedules and the checking of symptoms against the changes in the diets. In any test diet it is necessary to prove, by repeated tests, that the symptoms always occur when the food is taken and disappear when it is eliminated. When several foods are the cause of symptoms, the study is at times very complicated.

In order to simplify our study in allergic cases, we have for several years been using two very simple allergy test diets, which we have found to be of great help. Test Diet No. 1 consists of five foods commonly taken each day by the average normal person, namely: milk, egg, wheat, potato and either orange or tomato juice. These foods are combined into a basic diet in cases in which symptoms occur only intermittently, indicating an unusual food as the cause, and can be arranged to make a fairly well balanced though monotonous diet, as follows:

ALLERGIC TEST DIET NO. 1

Five foods only: milk, egg, wheat, potato, orange

Breakfast:
- One glass milk
- Dish of wheat cereal with cream and sugar
- Wheat bread and butter or toast
- Orange

Lunch:
- One glass milk
- Egg or cottage cheese
- Potato and butter
- Bread and butter
- Dessert: orange, orange flavored wheat pudding or custard

Supper:
- Same as lunch or breakfast
- Between meals and at bedtime: one glass of milk, with cream, glucose and wheat crackers
- Water: at least six glasses per day.

On such a diet one of three possible results may be encountered within two or three days:

(1) There may be no change in symptoms, indicating either that the offending food is one of the five foods ingested or that food allergy is not a factor in causing symptoms;

(2) The symptoms may be markedly exaggerated, indicating the presence of one or more offending foods in the diet;

(3) The symptoms may be ameliorated or may disappear entirely, indicating the absence of the offending food from the diet.

If the third result is obtained, new foods are added, one or two at a time, a record kept of the foods taken and any symptoms encountered, and any suspicious foods rechecked until all offending foods have been definitely determined.

If symptoms are the same or increased (results 1 and 2), we can either eliminate one food at a time until the symptoms disappear, later rechecking to make sure of results, or, preferably, Allergic Test Diet No. 2, containing none of the five foods of the first diet, may be substituted for it, as follows:

ALLERGIC TEST DIET NO. 2

Five foods only: rice, rye, 1 vegetable, 1 fruit, gelatin

Breakfast:
- Boiled rice or other rice cereal, with glucose
- Rye krisp
- Gelatin
- Fruit (raspberry)

Lunch:
- Vegetable (carrots)
- Rice
- Rye krisp
- Gelatin
- Fruit (raspberry)

Supper:
- Same as lunch or breakfast.
- Between meals and at bedtime: gelatin drink and rye krisp.
- Water: at least six glasses per day.

Plain gelatin powder may be taken in heaping teaspoonful doses, mixed with water or the fruit juice and sweetened with glucose.

Butter, which contains little or no milk protein, may usually be taken in moderation.

Boiled rice may be taken with butter and glucose, dry rice cereal with water and glucose.

This diet is not so satisfactory as the first, but the procedure to be followed is the same as for the first diet. Usually the offending foods can be rapidly ascertained by one diet or the other.

TREATMENT

Having determined the offending foods, the essential point in treating food allergy is to eliminate all of these foods entirely from the diet. When these foods are not essential to keep the patient's diet balanced or enjoyable, it is easy to avoid them for the rest of the patient's life if necessary. If, however, they are foods which

are taken normally in any rational daily dietary, such as milk, eggs and wheat, it is more difficult for the patient to eliminate them permanently, although he may be glad to do so at first. In such cases desensitization may be attempted. It is not necessary to start with hypodermic injection of purified proteins, as oral desensitization is usually satisfactorily accomplished. It is best to start with minute quantities of the foods each day, increasing the quantities gradually until symptoms reappear and finally arriving at a dosage beyond which the patient cannot go without getting symptoms, but usually large enough to permit of the taking of food mixtures containing small amounts of the food, as in the case of milk in cereal or coffee, egg in pudding or ice cream, or wheat in crackers or cake. In the case of milk, the initial dose in beginning desensitization should be one drop of whole milk; in the case of egg, one drop of a solution of a beaten egg in eight ounces of water or more; in the case of wheat, a small pellet made of bread. In this connection it is well to remember that when desensitization has been attained, the patient must take the acquired dosage of the food every day, as omission of the food for even a few days will re-establish the sensitivity. This fact makes it undesirable to desensitize any patient to a food which he would not care to eat each day or could not obtain at different seasons. Nonspecific desensitization by the use of peptone intravenously or by the employment of various forms of artificial pyrexia has been fairly successful in some cases, but in recent years has been rarely employed. The injection of increasing doses of histamine has also at times accomplished a nonspecific desensitization. In the past year or two histaminase has been tried, but this, in our hands, has rarely proven of benefit.

DIET

In planning the diet of the allergic patient it is well to bear in mind that a well-balanced diet is absolutely essential, that a normal vitamin and mineral content must be maintained, and that added vitamins or minerals of some kind may be indicated in the presence of grave deficiencies. A great danger is a low protein diet, and this must be carefully avoided. An intelligent patient will never cease to experiment with new foods and will find that sensitivities come and go. Seasonal variations may occur, especially in regard to milk, which may vary with the diet of the cow.

Aside from dietetic care, the allergic patient should have all focal infections eliminated, as at times allergy has been known to cease entirely after this procedure. Endocrine therapy may be indicated, especially the use of parathyroid hormone combined with calcium. Psychotherapy is often an important consideration. Local treatments, especially in the rectum, may be required, and the dietary principles in the treatment of any gastro-intestinal lesions should be followed as closely as possible, with operative procedures carried out as indicated.

In an attack of acute symptoms, as in a suspected "acute abdomen" or in severe ulcerative colitis, measures to meet the emergency must be instituted, among them being the following:

(1) Epinephrine, 1 to 1,000, 0.5 to 1 c. c., parenterally or sublingually, will sometimes give immediate relief of symptoms, although its occasional overstimulation of the thyroid may cause such severe symptoms as to contraindicate its use. At times ephedrine will produce a less distressing and fully as useful an effect, as may at times posterior pituitary extract or even parathyroid hormone and calcium. Epinephrine produces the best effect and may at times be instrumental in preventing a useless operative procedure.

(2) Except where an acute abdomen cannot be excluded as a cause of the symptoms, lavage and the cleaning out of the gastro-intestinal tract with castor oil or a cleansing enema is often of value to eliminate as much of the offending food as possible.

(3) Early and adequate feeding, avoiding foods apt to cause an allergic reaction, is important to stimulate normal gastro-intestinal function as early as possible and to prevent food deficiencies.

(4) In hemorrhage cases, or in very debilitated and anemic patients, transfusions are indicated and in ulcerative colitis are of especial value.

(5) In cases accompanied by perforation, obstruction or other serious complications, immediate operation may be necessary.

PROGNOSIS

With the elimination of all offending foods from the diet, the patient will be free of the symptoms of allergy, even though the symptoms of coexisting diseases may still be present. However, it is well to realize that an allergic patient is never static. He is always developing new manifestations from new foods and also losing sensitivity to former offending foods. Puberty, pregnancy and the climacteric may be accom-

panied by changes in or disappearance of allergic symptoms. Such a patient should therefore be under competent medical supervision always, especially when it is borne in mind that chronic irritation, which may be caused by constant ingestion of allergenic substances, may possibly be a factor in causing gastro-intestinal malignancy.

SUMMARY

(1) Gastro-intestinal allergic manifestations are commonly seen and frequently not recognized.

(2) The pathology of the allergic reaction in the gastro-intestinal tract has been demonstrated.

(3) Severe allergic reactions may simulate serious acute abdominal disease and may result in unnecessary operative interference.

(4) Allergy being a frequent accompaniment of other gastro-intestinal lesions, a complete gastro-intestinal study is necessary before allergy is treated.

(5) Elimination of offending allergic factors constitutes the principal therapeutic procedure.

(6) An adequate, well-balanced diet is necessary in all cases.

(7) General hygienic care and attention to all other diseases is essential.

REFERENCES

1. Andresen, A. F. R.: Med. Jour. & Rec., —:— (Sept. 2) 1925.
2. Gray, I.; and Walzer, M.: Amer. Jour. Dig. Dis. & Nut., **14**:11 (Jan.) 1938.
3. Walzer, M.; Gray, I.; and Harten, M.: Abstracted in Jour. Allergy, **9**:394, 1938.
4. Walzer, M.; Gray, I.; Strauss, H. W.; and Livingston, S.: Jour. Immunol., **34**:91, 1938.
5. Kallos, P.: Gastroenterologica, **64**:234, 1939.
6. Fries, J. H.; and Zizmor, J.: Jour. Ped., **16**:69, 1940.
7. Kaijser, R.: Arch. Klin. Chir., **188**:36, 1937.
8. Afendulis, T. C.; and Gullzow, M.: Zeitschr. f. d. Exper. Med., **104**:167, 1938.

88 Sixth Avenue

DISCUSSION (*Abstract*)

Dr. Warren T. Vaughan, Richmond, Va.—There is a definite difference between the early papers on gastro-intestinal allergy and Dr. Andresen's present excellent discussion. The former described symptoms and their apparent cause and effect relationship with exposure to specified allergenic excitants. Dr. Andresen has told us of the pathologic lesions themselves, their microscopic appearance, and their gross pathology, as brought out by experimental studies and radiologic examination. Our understanding has advanced apace.

Dr. Andresen's two diets are quite different from those previously recommended. Each allergist would probably make slight modifications in Diet II, dependent on his local problems, but his Diet I, milk, eggs, wheat, potato and orange, appeals to me very much as a trial diet with which quickly to settle the question of allergenicity of these staples. I plan to try it.

There is only one point on which my experience differs from that of Dr. Andresen. He states that "sensitivity is constant and qualitative." Even a very small quantity of an allergen will give a reaction whenever taken, so that failure to show a reaction after ingestion of a suspected food rules out that food as a factor in the problem."

Our experience, on the contrary, has been that one of the great difficulties in many cases is that one may tolerate a food at one time, but have trouble from it at another. This increases the difficulty of detecting the culprit.

Dr. Seale Harris, Birmingham, Ala.—Dr. Andresen made me conscious many years ago of the fact that food allergies are frequently met with in patients complaining of gastro-intestinal symptoms. I am sure that gastro-intestinal allergy occurs frequently in such patients and that in overlooking it we fail to give our patients relief in many cases. Brief report of a severe case of generalized eczema associated with a duodenal ulcer will illustrate a type of gastro-intestinal allergy. Dr. Marion Davidson, of Birmingham, referred to me the patient, a woman about 40 years of age, whom he had found to be sensitized to many foods, including milk and wheat. I had difficulty in working out a diet for the duodenal ulcer, proven by x-ray examination, because she was allergic to many foods commonly included in ulcer diets. With the elimination of the foods to which she was sensitized and on a modified ulcer diet adjusted to her nutritional needs, she recovered from the ulcer and the severe generalized eczema, and she has had no symptoms of either the eczema or the ulcer for four or five years. After a few months she found that she could take milk without bringing on allergic symptoms and she takes it regularly now. This brings out a point which Dr. Andresen emphasized, namely, that a patient may be sensitized to various foods at times and in a few months the allergy may pass off.

The relationship of allergy to hyperinsulinism (spontaneous hypoglycemia) has been discussed by several clinicians. We have not reported the cases, but we have found low blood sugars in several patients who had gastro-intestinal symptoms, and who were allergic to various foods. An allergist of Dallas, Texas, reported that nearly 50 per cent of a series of asthma and hay fever patients had low blood sugars; and two Viennese clinicians, before Hitler took over Austria, reported a number of cases of allergy associated with spontaneous hypoglycemia.

If gastro-enterologists would make blood sugar studies in their cases of gastro-intestinal allergies they might find that spontaneous hypoglycemia is a factor in some of them.

The relation of endocrine disorders to allergy has been studied by a number of clinicians and there are many reasons to believe that hypo-adrenalism may play a part in the etiology of food sensitization. The fact that the administration of epinephrine, or ephedrine, often relieves asthma and some of the skin manifestations of various allergies certainly suggests that in such cases there may be a deficiency of the internal secretions of the suprarenal glands. It will be recalled that spontaneous hypoglycemia is also a manifestation of

hypo-adrenalism. Since epinephrine and ephedrine raise blood sugar levels, the thought occurs to me that perhaps in asthma and other cases in which there is allergy, hypoglycemia may be a factor in some cases.

Dr. Morris Shushan, New Orleans, La.—There are two points that I should like to emphasize in this connection. The first is the pyschogenic factors and their connection with food allergy. In my experience psychogenic factors operate in several ways. I believe that a great many patients are primarily and fundamentally problems in food allergy. After a period of years, however, with many attempts resulting in unsuccessful therapy, they develop an anxiety syndrome. They then present a combination of food allergy and psychoneurotic manifestations. If one can gain their confidence, and limit their diet in the manner shown by Dr. Andresen, one can accomplish a great deal.

It has been my experience that allergy may be conditioned by psychic behavior patterns. I have seen patients who, during periods of great emotional tension, passing through unusual experiences, developed allergic symptoms; later on, when conditions were more stable, they would show no food allergy.

This could be illustrated by many case presentations, but I believe that this factor is responsible for patients showing evidences of food sensitivity at one time and then later on being able to take the same foods without any trouble.

In certain cases of colonic allergy I believe that smears from the rectal mucosa, stained with Wright's stain, are a definite aid in diagnosis. Bercovitz has been interested in the subject of making smears from the rectal mucosa, but I believe a Wright's stained preparation should be added to his technic.

In my experience, many food allergies with colonic symptoms, if proctoscopic smears are stained, will show eosinophils, as in the nasal mucosa and the sputum. The appearance of the rectal mucosa is very frequently characteristic, and if one finds a yellowish mucoid exudate, those smears will nearly always be found to contain eosinophils.

Dr. Andresen (closing).—Dr. Vaughan has disagreed with my statement that if a patient fails to get a reaction within twelve to twenty-four hours after ingestion of a food, that food can be considered one to which he is not sensitized. He said that patients might show variations in regard to reactions to foods to which they are really sensitized. I have observed this also, but in most cases careful study will reveal some other unsuspected cause of the reaction which is not present when no reaction occurs. As was pointed out in the paper, there are factors which influence sensitivity. Patients may show allergic reactions only during menstruation or pregnancy, emotional states may be accompanied by allergic reactions, or a summer sun tan, with its influence on blood calcium and vitamin D, may reduce sensitivity. The method of preparation of a food may also account for its producing a reaction at one time and not at another, the patient being really sensitive to some addition made during the preparation, such as condiment with lettuce, or the boiled egg garnish on spinach.

Variations in the location of the allergic reaction make allergic patients interesting studies. I remember a patient whom your Secretary has seen. We saw her first when she had symptoms suggesting an "acute abdomen," but as she had had two previous laparotomies for such episodes we were suspicious of allergy and gave her epinephrine, which was followed by prompt relief. After elimination of foods to which she had been shown to be sensitized, she disappeared, but later I heard from her that she was being treated for angina pectoris. I suggested an allergic study and the cause of the anginal attacks was discovered. Later she moved to New Orleans, where Dr. Browne subsequently found a diarrhea to be due to sensitization to pompano.

I agree with Dr. Shushan that the psychic disturbance is usually the result and not the cause of the prolonged gastro-intestinal symptoms. Usually it will clear up with improvement in the patient's general condition. We had a milk-sensitive patient with severe ulcerative colitis last winter, who had a marked degree of psychic reaction. His bowel cleared up slowly on elimination of milk from his diet, but he was still quite neurotic. When his symptoms had entirely cleared up we attempted to desensitize him to milk, starting with drop doses. On reaching seven drops he had a severe bowel reaction, which the intern thought was due to the patient's knowledge that he had received milk, and thus purely psychic in origin. Therefore, when the bowel was again normal, symptomatically and proctoscopically, we concealed seven drops of milk in his food one day. Although he knew nothing about it, he was disturbed all the following night with a profuse, bloody diarrhea. The intern was convinced.

We have had but little experience in searching for eosinophils in rectal smears.

RECURRENT EROSIONS OF THE CORNEA*

By MAXWELL THOMAS, M.D.
Dallas, Texas

The title, "Recurrent Erosions of the Cornea," has been chosen because it is a term that can be applied to a number of allied conditions which have a similar symptomatology and pathology, although the etiologic factors may be entirely different. Such recurrent lesions of the cornea offer a problem of no little moment which taxes our diagnostic acumen. A definite understanding of the term, erosion, is needed, and the master ophthalmologist Fuchs[8] offers pathologically one of the best, namely: "A superficial excoriation of the cornea which simply produces a loss of substance in the epithelial covering." However, clinically the etiology with the symptomatology which accompanies the exposure of the nerve endings should be included as part of any definition.

Because erosions tend to produce a definite

*Read in Section on Ophthalmology and Otolaryngology, Southern Medical Association, Thirty-Fourth Annual Meeting, Louisville, Kentucky, November 12-15, 1940.

complex of symptoms, this should be referred to as recurrent erosion syndrome, and each case should be classified according to the ascertained causes when possible.

Most of the observations upon this condition have been clinical; therefore, efforts have been made to name the type according to the etiology. This was probably the reason Lloyd[17] found it convenient to discuss such a condition under the subject of "Herpes and Allied Conditions," whereas Buffington[3] places cases of herpetic type under the classification of neurotrophic keratitis. In the German literature there has been a more definite trend to refer to the condition as traumatic herpes of the cornea, but this would hardly have been a logical diagnosis before the discovery of the herpes virus by Grüter[13 14] in 1912. Terms used by older authors, such as the intermittent keratitis vesicularis neuralgica of Hansen[16] in 1852, no doubt were descriptive of the present recurrent erosions. The term relapsing traumatic keratitis of DeSchweinitz[5] likewise fits in this same picture. All have described essentially similar pathologic processes of the cornea.

ETIOLOGY

A search for the etiology of recurrent erosions was intensely interesting, as most observers have given purely clinical names to the pathologic condition which they have seen. This has been done from an etiologic or symptomatologic, rather than pathologic viewpoint without any definite regard to the existing condition. Therefore, the etiologic terminology includes both definite and indefinite terms. We find in the literature the spontaneous type as a result of heredity, according to Franceschetti[7] and a case reported by Schappert[25] in which the family for three generations had had degenerative lesions of the cornea with erosion, indicating an hereditary basis. Furthermore, systemic disturbances have been accused as A. Vogt[31] drew the conclusion that herpes was mostly a symptom of general disease. A bizarre report was made by Spektor,[26] who described recurrent erosions from intestinal worms (Ascaris).

Salus[24] describes a spontaneous variety of recurrent erosion, the clinical picture of which was identical to that seen in the traumatic variety.

Finding no real cause and with a desire to place responsibility for the condition upon something locally present in the cornea, Peters[21] in 1903 and again in 1930,[22] after the discovery of the herpes virus, reaffirmed his belief that the neurotrophic disturbance provides a point of attack for the neurotrophic virus acting endogenously.

McNabb[19] reasoned that the bulk of abrasions and slight injuries of the cornea completely recover without subsequent trouble; yet there must be a causal factor of a neurotrophic nature when they do not. He commented that some surgeons stress the neurasthenic element.

Allergic reaction has been duly named as a cause and probably there is no better illustration than that seen in the manufacture of artificial silk as described in Duke Elder's "Textbook of Ophthalmology."

Intra-ocular disease with injury to the endothelium and Descemet's membrane are likely to be accompanied by changes in the epithelium with recurrent erosion. This no doubt was the reason for Gifford's[9] article in which attention was called to the probable relation between recurrent erosion of the cornea and Fuch's epithelial dystrophy.

Trauma as an actual and exciting cause of recurring lesions of the cornea is well recognized. Terry[30] said:

> "Should either epithelium or endothelium be injured water passes freely, giving rise to swelling of the substantia propia due to its turgescence and to edema of the cornea with subepithelial vesicle formation."

When such a process continues long after the normal time for healing, damage must have occurred to the nerves so that, according to Gifford,[9] a neurotrophic disturbance prevents normal reattachment of the epithelium. Trauma alone must be the cause when such erosions continue to reappear proximal to the site of actual injury.

Herpetiform disease of the cornea has a symptomatology quite like that of any recurrent erosions, and with trauma as an exciting cause the clinical and pathologic picture is quite confused. So true is this that in the literature trauma as a separate cause is relatively rare; instead, traumatic herpes is the common term found, but there is usually doubt as to just what part trauma plays and what part the complicating herpes plays. Because of this E. Ammann[1] compiled a review on traumatic herpes for the Swiss law governing accidents and indicated that trauma was the exciting cause, but that the actual cause of the pathologic changes which followed were from the herpes. He suggested an arbitrary

clinical method for establishing the cause as traumatic or herpetic disease.

In an effort to obtain the incidence of recurrent erosion from trauma among the statistical studies, those made of the subject of posttraumatic herpes by Lueg gen. Althoff,[18] Brandis[2] and F. Stocker[27] were examined, but these were not conclusive.

The suggested causes of recurring erosion are numerous and no doubt others could be added to those named. Nevertheless, regardless of the cause, the corneal changes in recurrent erosions appear to follow certain pathologic stages.

PATHOLOGY

There is a scarcity of pathologic studies upon human eyes with recurrent erosion other than the study of corneal scrapings. Meighan[20] was one of the few to obtain sections of an eye for study, but little more information was given than that obtained with the corneal microscope.

Biomicroscopy in recurrent erosions is the one method of studying the pathology, and this method presents a picture not unlike Rones'[23] description of corneal edema. The first evidence is the presence of a swollen edematous area with only a faint haze to indicate the change. No staining is seen early, but eventually the areas stain, depending upon when the vesicle ruptures or the epithelium desquamates. A few hours to several days may elapse before any fluid forms a vesicle in such areas. These vesicles are of varying sizes; the very small ones may even escape notice and are superficial in the epithelial layers, whereas larger vesicles are between the elastic lamina and Bowman's membrane. The small ones rupture and heal before staining can reveal the existence of an erosion. The larger ones may persist for a longer period, but they rupture and heal quickly so that the unpleasant symptoms vanish rapidly, due, no doubt, to the nerve endings' receiving protection by overgrowth of epithelial cells. This process of epithelization is so prompt that there is an illusion of rapid healing. There is some surprise when the epithelium is easily removed, and it may peel off over a much larger area than was expected. Certainly this means that there exists some disturbance in the normal adhesive qualities of the epithelium to Bowman's membrane, allowing repeated disjunction of the epithelium, a term used by v. Szily.[29]

The location of eroded areas is most interesting. The epithelium always erodes proximal to the site of injury or where a previous abnormal condition has existed. This is especially true in traumatic cases where the deeper layers of the cornea and the endothelium have been injured. In cases in which lesions seem to be scattered and confined to the epithelium, the complication of an existing herpetic infection is to be suspected.

SYMPTOMATOLOGY

The symptoms of the syndrome of erosion are quite classical and it is the fact that they repeatedly occur which gives the title to this paper. The story is typical; the patient on awakening or opening the lids after a few moments' closure experiences a sharp pain in the eye which radiates over the side of the head or remains in the eye proper. With this effort to open the eyes tears flow so freely that they must be wiped away. Marked sensitivity to light gives the impression that the bright light is the cause of the trouble. The eye may be slightly reddened, but usually once the eye is opened the discomfort passes away, and only the sensation of a foreign body remains. Probably this is due to the fact that the lids stick to the blebs or pull on the edematous corneal epithelium, exposing or irritating the nerve endings.

Corneal sensitivity was found lowered in the forms of the disease which have the pathologic changes confined to the epithelium. Certainly with the injury to the nerve endings directly by trauma or by infection with the herpes virus, hyperesthesia would not be the most prominent symptom.

Hyperesthesia, if it does exist, at times may account for the complaint of headache over the affected side, often referred into the temporal region, which comes on from a few hours to days before the corneal epithelium breaks down to form a bleb and subsequent erosion. Immediately after the formation of the erosion, some lowering of corneal sensitivity seems to exist in the affected eye as compared with the uninvolved eye. It has also been observed that after the bleb breaks, the pain around the eye may not leave completely but does subside.

PROGNOSIS

The prognosis is relatively good when the erosions appear to have their cause within the epithelial layers. However, if cases of herpes are neglected so that the parenchyma is invaded, scarring will be the result. When the endothelium is damaged as in epithelial dystrophy loss of vision due to the scarring always occurs. A secondary invading organism will likewise alter

the prognosis, and in some cases even the globe will be lost as was true in *Case 1*. Early determination of the etiology with proper treatment in most instances will alter the course of this stubborn condition with little loss of vision.

TREATMENT

Treatment of all cases should have the distinct aim of removing all diseased epithelium and the making of a sound bed for the growth of healthy and new epithelium. When no reasonable cause is found, the search for a focus of infection or systemic process with their elimination is of a paramount importance. When the erosion is non-traumatic and herpes is eliminated, it may be assumed that the cause is neurotrophic. Locally the use of bland oils in the conjunctival sac and a mild antiseptic to avoid secondary infection will suffice. Here would be indicated the use of various vitamins, especially A and the B group.

Cases in which trauma may be incriminated need protection and the use of a mild cauterant, such as iodine, upon eroding areas will help to restore a normal adherence of the epithelium and when applied early to returning lesions will probably destroy any chances of the herpes virus' becoming active.

Most types of acid have been used, regardless of the cause of the erosion. Strader[28] and Jackson used carbolic and nitric acids. This seems somewhat drastic, especially in cases in which the lesion is near the pupillary area. When a mild destructive agent is needed and the existence of a corneal haze is not of any consequence, trichloracetic acid may be used.

Certainly if the herpes virus is suspected, iodine is the therapeutic agent of choice, using it as Gifford[10] suggested in a paste, or even a strong iodine solution as advocated by Gunderson.[15] In either event some of the normal tissue must be destroyed, and, according to Gunderson, no permanent damage is done to the deeper corneal layers. In the discussion of Gunderson's paper, Goar[11] advocated a thorough curettement and then the application of iodine. In this thought the author most wholeheartedly concurs, and in order to avoid injury to the deeper structure a dull curette and a capsule forcep will save time and trauma.

Greeves[12] has suggested the use of x-ray and has given the dosage. He says that although carbolic acid and other cauterants seem to check the erosions, they have a disadvantageous scarring effect in the pupillary area. For this reason x-ray is more suitable.

CASE REPORTS

The following collected case reports are typical examples of recurrent erosions of the cornea. In *Case 1* it has been impossible to find an etiologic cause. *Case 2* is due to trauma, with a proven herpetic disease complicating the picture. *Case 3* is included because trauma was the only thing that could be found as a cause. *Case 4* deals with a patient in whom there was an alleged trauma to one eye without any trauma to the other eye. The neglect in treating it had produced the marked changes in the corneal stroma. Brief comments follow each case report.

Case 1.—Miss D. N., a white woman, aged 39, reported with the history of having lost her left eye in 1931, following a year of illness with a peculiar malady of the cornea which came and went until at last an ulcer of serpigenous variety caused the globe to be lost. At that time similar symptoms of a foreign body and pain over the side of the head with lacrimation existed. In April, 1934, examination of the remaining eye revealed an appearance identical to that of the eye lost in 1931. There was an edema of the corneal epithelium just below the pupillary area, and a number of small vesicles which eventually fused into one large bulla which ruptured. The vision naturally was reduced to 6/10. The refractive error was plus 5.00 S, the intra-ocular tension was normal to palpation, and when the eye had recovered it registered 21 mm. Hg. McLean. The eye healed under conservative treatment of hot applications, antiseptic solution, a mild ointment for relief of pain, and protection with a moisture chamber.

Never again subsequently, did such a large bulla form. However, in this same area and to each side of the original lesion, which left a faint scar, other vesicles appeared. An attack occurred in April, 1936, another in November, 1936. It was nearly two years before she returned in July, 1938, with another attack and again in December the same year. In April, 1939, only a small erosion which lasted seven days was present. The last time she was seen was in May, 1940, when she appeared with a very small vesicle. The vision has remained at 9/10 of normal.

This case represents the spontaneous type of erosion with attacks which have come principally following prolonged use of the eyes and when the patient's general health has been under par. That some mild trauma as an exciting factor plus corneal areas of lowered resistance were the cause would be hard to deny, as the erosions have always occupied areas of the cornea at the site of former erosions or next to them.

Case 2.—Mr. A. Y. T., a white man, aged 25, on September 7, 1939, cut the right eye with a piece of corrugated cardboard. Over the phone his family physician prescribed an anesthetic ointment which partly controlled his discomfort. Three weeks later the chief complaint was the tearing and burning of the eye each morning with a marked photophobia and sticking sensation. No secretion was ever present, but still he had difficulty in opening the lids.

The past history was of no significance. Recurrent multiple lesions scattered here and there away from the site of the original lesion were generously touched with tincture of iodine. In spite of this the patient continued to have trouble occasionally with erosions here and there over the cornea. Consultation was obtained as to a radical procedure of removing all the epithelium and the patient disappeared from observation for two months.

On return, the lesions were numerous and generously scattered. A physical examination was requested which yielded negative results. A thorough laboratory check revealed no positive findings except herpetic lesions which were reproduced from scrapings on to a rabbit's cornea.

Ocular examination of the right eye on the patient's first visit showed a healed lesion of the cornea at 3 o'clock 2 mm. from the limbus. Just below this area was a small vesicle, 1 mm., one end of which seemed to stain. In 24 hours this had disappeared and the sensation of a foreign body also had passed. There remained a slight haze and elevation of the epithelium. Some ten attacks were observed with difficulty in finding even a vesicle or staining area when the patient was first seen. Eventually there appeared a vesicle or vesicles, with a breakdown and the formation of an eroded area of very irregular outline, confined entirely to the swollen epithelium which surrounded it. The sensation of the cornea was markedly diminished when the vesicle broke.

When iodine was applied recovery promptly started, and the time between attacks was lengthened. Like the small lesions seen in a dendritic keratitis these lesions appeared. All the epithelium was removed by means of forceps and a strong solution of iodine applied to the denuded areas. Some months have passed without a recurrence though the total period of trouble extended from September to March the following year. There was no visual loss.

This case is a typical example of recurrent erosions of a relapsing keratitis, of the herpetic type. Trauma was unquestionably the exciting cause as was evidenced by the slight scar seen. The fact that all the pathologic tissue remained confined to the epithelium and the erosions were multiple and generously scattered, suggested the herpes virus as the cause for recurrence. This, of course, was confirmed by animal inoculation.

Case 3.—Mr. N. B., a white man, aged 28, suffered injury to both eyes in an explosion of a glass window from an air line. The shattered glass struck both eyes, inflicting many scratches, abrasions and cuts with perforation of the left cornea and limbus at 7 o'clock and slight prolapse of the iris at the perforation. The right bulb was not penetrated. The left eye healed rapidly and in less than one month all inflammation had subsided. The right eye remained red, but the tension of both was 22 mm. Hg. McLean. The vision in six weeks had arisen to approximately 10/10 in each eye. Every few weeks the right eye became markedly inflamed, sensitive to light, with marked lacrimation, and with the sensation of the presence of a foreign body.

For 18 months erosions of the cornea continued so that the following brief description would apply to any attack the patient suffered. In spite of the apparently severe injury to the left eye no further trouble was experienced. The right eye, however, showed numerous scars of the cornea, over the surface of which the epithelium seemed piled up and several repeatedly eroded areas developed near the corneal scars, in one area 1.5 mm. from the limbus at 1 o'clock. The endothelium was thickened; also, numerous folds in Descemet's membrane were present, extending from the described area. This was worse when a vesicle was seen. Only an occasional cell was seen in the aqueous. The corneal nerves were more prominent than usual, standing out in comparison to the other eye. The fundus was clear as was the refractive media. When the patient was seen from time to time, the edema of the cornea and wrinkles in Descemet's membrane were subsiding. With each inflammatory attack the picture described reappeared but not without the formation of an occasional vesicle at the sites of injury. These attacks gradually diminished in number.

Laboratory examinations were negative, including inoculation of a rabbit's cornea with scrapings. The tuberculin test was negative. Iodine was used to touch up the eroded areas from time to time. Foreign protein injections, dionin, and always rest and binding up the eye helped to relieve the symptoms and aided the eye to clear up.

This is a case of traumatic recurrent erosion due largely to deep corneal injury and probably also due to neurotrophic changes as a result of disturbance in the sensory nerve endings. The erosion was preceded not only by a definite vesicle but by the heaping up of the epithelium which was torn off by action of the lids over the eyeball. The patient recovered after a period of one and one-half years. It was of increasing interest in this case that there was a parallel course of erosions and vesicle formation with the endothelial disturbances. It is in accord with Cogan,[4] to quote:

"Moreover, the superficial vesiculation is localized to that portion of the cornea corresponding to the disturbance of the posterior portion, so that there can be little doubt of a connection between the epithelial and endothelial changes."

Case 4.—Mrs. O. S., a white woman, aged 43, February, 1937, said a skim came over the left eye following a scratch of the eye that seemed quite trivial. The eye was treated but did not seem to improve. The right eye became affected without any history of trauma, but it gave her only slight trouble.

The symptoms were somewhat typical as she had a marked photophobia and some pain which came and went, varying in severity. The sensation of a foreign body was constant. However, as soon as lacrimation was excessive she could open the eyes, a procedure which was most difficult in the mornings. This process continued for six months but seemed to be partially controlled when the epithelium, which was loose, was removed and the area cauterized with trichloracetic acid.

All laboratory findings were normal except for a slight anemia. A careful physical check likewise revealed no abnormalities.

Ocular examination of both eyes with a loupe revealed

a hazy area with its center just below the pupil in each eye with a more extensive area on the left. In the center of each a small area stained, and with the slit lamp there was a definite edema of the epithelium and a cloudiness of the adjacent parenchyma extending one-third the thickness below Bowman's membrane which was no longer definite in outline. At various examinations the outlining areas seemed to consist of small vesicles which had coalesced. All the epithelium could be wiped away quite easily at times, depending upon the stage of the lesion. The right eye responded to iodine and seemed to heal. The left was resistant, and for nearly ten months she was not seen but was under the care of a colleague who repeated just this treatment. At the end of that time she was seen and the process seemed to have halted. However, scarring extended down rather deeply into the parenchyma and the healed epithelium had a rough appearance. When the patient was last seen in February, 1940, the vision was reduced to right eye 6/10, left eye 4/10.

This case has been presented as an example of neglected erosion with alleged trauma in one eye but no history of trauma in the other eye, indicating the probable existence of neurotrophic changes which allowed the entrance of the herpes virus in the more inflamed eye. The right eye was apparently a spontaneous variety in which the etiology remains idiopathic; no cause was ascertained.

SUMMARY

"Recurrent erosions" is a term describing a type of corneal disease which has a definite group of symptoms. For this group of allied conditions the name recurrent erosion syndrome is proposed as this is not a clinical disease entity.

The only manner in which to classify this syndrome is to designate the etiology, although this is neither wholly satisfactory nor always possible.

Parallelism in stages of corneal changes regardless of cause produces a characteristic symptomatology due to erosions of the epithelium.

Prognosis should be guarded when treatment proves ineffective.

Treatment is successful when prompt. The chief aim is the elimination of the cause and the establishment locally of a firmer adherence of a healthy epithelium.

Four case reports are included to illustrate some of the changes described.

BIBLIOGRAPHY

1. Ammann, E.: Herpes traumaticus und Art. 91 K.U.G. (Traumatic Herpes according to Specifications of Swiss Law Governing Accident Insurance). Schweiz. med. Wchnschr. (Aug. 19) 1933.
2. Brandis, Heinz: Zur Frage des Herpes Cornea traumaticus. inaug. Diss., Marburg; 1936.
3. Buffington, W. R.: Keratitis: Nutritional, Neurotrophic, Dystrophia. Sou. Med. Jour., **24**:300-309 (April) 1931.
4. Cogan, David G.: Experimental Production of So-Called Bullous Keratitis. Arch. Ophth., **23**:918-925 (May) 1940.
5. DeSchweinitz, G. E.: Relapsing Traumatic Bullous Keratitis, with Cases. Ophthalmic Record, **11**:76, 1902.
6. Elder, Duke: Textbook of Ophthalmology, **11**:1709. St. Louis: C. V. Mosby Co., 1938.
7. Franceschetti, A.: Hereditaere rezidivierende Erosion der Hornhaut (Hereditary Recurrent Erosion of the Cornea). Ztschr. f. Augenheilk., **66**:309, 1928.
8. Fuchs, E.: Textbook of Ophthalmology Duane, 8th ed., p. 579, Philadelphia and London. J. B. Lippincott Co., 1924.
9. Gifford, S. R.: Epithelial Dystrophy and Recurrent Erosion of the Cornea as Seen with the Slit Lamp. Archives Ophth., **54**:217, 1925.
10. *Idem.* Hand Book of Ocular Therapeutics, 2nd Ed., p. 191, Philadelphia: Lea & Febiger.
11. Goar, Everett L.: Discussion, Herpes Corneae. Arch. Ophth., **15**:248, 1936.
12. Greeves, R.: Affleck: X-ray Applications in Superficial Keratitis. Trans. Ophth. Soc. U.K., **5**:11, 1930.
13. Gruter, Wilhelm: Cited from Brandis, Heimz-Zur Frage des Herpes Corneae traumaticus. Inaug. Dis. Marburg, 1936.
14. *Idem.* Das Rezidiv bei den herpetischen Erkrankungen der Hornhaut. Ber dtsch. Ophthal. Ges. **45**:104, 1925.
15. Gunderson, Frygue: Herpes Cornea. Arch. Ophth., **15**:225-248, 1936.
16. Hansen: Cited from Duke Elder Text Book of Ophth., vol. 2, p. 1852. St. Louis: C. V. Mosby Co., 1938.
17. Lloyd, Ralph K.: Herpes and Allied Conditions. Amer. J. Ophth., 3rd Series, **14**:601 (July) 1931.
18. Lueg gen. Althoff, Reinhold. Untersuchungen uber die Haufigkeit des traumatischen Hornhaut herpes. Inaugural Dissertation, Bonn, 1935.
19. McNabb, H.: Recurring Erosions of the Cornea. Trans. Ophth. Soc. United Kingdom, **53**:500, 1938.
20. Meighan, Spence: Two Cases of Relapsing Traumatic Vesicular Keratitis. Trans. Ophth. Soc. United Kingdom, **44**:46, 1924.
21. Peters, A.: Ueber traumatische Hornhauterkrankungen (Erosionen, Keratitis discifirmis und Ulcus serpens) und thre Beziehungen zum Herpes corneae. Arch. f. Ophtha., **57**:93, 1903.
22. *Idem.* Klinisches zur Frage der rezidivierenden Erosionen und des Herpes corneae (Clinical Study of Recurrent Erosions and of Herpes of the Cornea). Klin. Monatsbl. f. Augenh., **85**:640-644, 1930.
23. Rones, Benjamin: Pathologic Conditions of the Cornea. Arch. Ophth., **24**:374-395 (Aug.) 1940.
24. Salus, Robert: Ueber traumatische und nichttraumatische rezidivierende Epithelerkrankung der Hornhaut. (On Traumatic and Non-traumatic Recurrent Disease of the Corneal Epithelium). Klin. Monatsbl. f. Augenheilk., **68**:673, 1922.
25. Schappert-Kimmijser, Joha.: Recidiveerende Hoornvlieserosie en Familiaire Hoornvliesdegeberatie (Recurrent Erosion of the Cornea and Familial Degeneration of the Cornea). Nederl. Tijdschr. f. geneesk., **77**:992 (March 4) 1933.
26. Spektor, S.: Klinisches zur Frage der Aetiologie von doppelseitigen rezidivierenden Erosionen der Hornhaut (Clinical Studies of the Etiology of the Bilateral Recurrent Erosions of the Cornea.) Klin. Monatsbl. f. Augenheilk, **87**:661, 1931.
27. Stocker, F.: Zur Frage der Traumatischen Ausloesung des Herpes Cornea (Trauma in the Causation of Herpes Corneae). Schweiz. med. Wchnschr., **51**:610-615 (June 30) 1931.
28. Strader, G. H.: Recurring Corneal Bleb. Ophthalmic Record, **18**:86, 1909.
29. v. Szily (Sen.) A. f. O., **51**:486, 1900.
30. Terry, Theodore L.: Some Physiological and Anatomical Aspects of the Cornea Affecting Its Pathology. Amer. J. Ophth., **22**:153-155. (Feb.) 1939.
31. Vogt, A.: Zur Stellung des Herpes corneae febrilis (simplex in der Unfall-Ophthalmologie (The Place of Herpes Corneae Febrilis (simplex) in Traumatic Ophthalmology. Schweiz. med. Wchnschr., **57**:481-483 (May 21) 1927.

Medical Arts Building

DISCUSSION (*Abstract*)

Dr. J. Wesley McKinney, Memphis, Tenn.—The "recurrent erosion syndrome," as Dr. Thomas has pointed out, is not a disease entity, but a manifestation of a number of pathologic conditions of the cornea.

According to my experience, corneal erosions have occurred most frequently in connection with long-standing glaucoma, chronic uveitis and old corneal opacities,

whether traumatic or infectious in origin. Less frequently erosions accompany corneal dystrophies, herpes, neuroparalytic conditions, deep-seated corneal inflammations and postoperative aphakia in which there has been loss of vitreous or in which vitreous has remained permanently in contact with the back of the cornea.

Clinically, corneal erosions are always associated with edema and vesiculation of the epithelium. No theory has been able to explain the pathogenesis of the edema, vesiculation and erosion which may occur with so wide a variety of conditions. The fact that in most cases hypesthesia is present, suggested a neurogenic basis. The fact that many cases were associated with an endothelial disturbance suggested that the dehiscent or diseased endothelium allowed aqueous to filter through the cornea and to fill the spaces beneath the relatively impermeable epithelium. These two most generally accepted theories seem to fit many cases, but neither explains all the elements involved.

Recently Cogan (*Archives of Ophthalmology*, 23:918, 1940) conducted a series of experiments which indicate that the fluid which causes the corneal edema may be derived from without the eye. Enucleated dogs' eyes were placed in 2.5, 10 and 20 per cent solutions of sodium chloride. After thorough saturation in the hypertonic solutions the eyes were placed in water or physiologic saline for varying lengths of time. The result was first, epithelial edema, then vesiculation, then the formation of bullae and finally the entire epithelium became detached. In another experiment the hypertonic saline was injected into the anterior chamber and then the eyes were immersed in water or physiologic saline. The results were the same. Interestingly enough, the process was reversible. After the bullae had developed the eyes were immersed in a hypertonic solution. Within a few minutes the bullae disappeared and the cornea became clear again.

According to these experiments, the mechanism of corneal edema, vesiculation and erosion is an osmotic attraction of fluid into the cornea from the outside. If these facts may be applied clinically, it would seem to indicate the use of hypertonic solutions to combat corneal edema until the balance between the osmotic tension of the intra-ocular fluids and the tears could be re-established.

In the realm of my own personal experience, there are two therapeutic agents whose value I should like to emphasize. The first of these is x-ray therapy. Most cases of corneal erosion will respond to the usual procedures of protection, ointments and the application of iodine or trichloracetic acid. In some instances the edema, vesiculation and recurrent erosion persist. It is for these resistant cases that I have often found the use of stimulating doses of x-ray to be curative. A single case will serve to illustrate:

A 44-year-old man gave the history of repeated erosions of the left cornea for the preceding eight years. These erosions would appear day or night and last for a day or so, and clear up whether treated or not. Recurrences continued despite the use of many ointments and applications. There was a superficial nebulous scar about 4 mm. in diameter in the center of the cornea. The cause of this scar, which had been present since childhood, was unknown. The slit lamp revealed mild epithelial edema and vesiculation over the scar. There was no other ocular disease, and all foci of infection had been removed. He was finally advised to have x-ray therapy. He was given weekly treatments consisting of the application of 60 r. The edema and vesiculation gradually disappeared and he has now been free of erosion for eighteen months.

An important principle in the treatment and prophylaxis of recurrent erosions is that of protection. This is ordinarily obtained by means of bandaging. Certain cases in which the corneal sensitivity is lowered require protection for long periods of time. A convenient means of obtaining this protection is by use of the Tovell eye shield. This shield consists of heavy cellophane fitted between the lens and rims of an ordinary pair of spectacles. The short tube of cellophane thus formed is cut to conform to the contours of the face. This device has been found particularly valuable in preventing neuroparalytic keratitis after nerve root resection for trigeminal neuralgia.

Dr. F. B. Blackmar, Columbus, Ga.—This condition can be extremely trying on occasions. Recently I treated a case where I was pulled out of a hole by a suggestion from Dr. Thigpen, of Montgomery.

A patient with corneal erosions had been struggling along for about a month without indication of improvement. We used vitamins, foreign proteins, bandage, removed epithelium, applied iodine, and after all my efforts, he was just about where I started. He was getting a little apprehensive and suggested he would like to see Dr. Thigpen. This met with my approval and I hoped he would keep him, but he sent him back and, to my astonishment, said he never had much trouble with these erosions and just treated them as cases of conjunctivitis with silver nitrate on the lids.

As usual in these cases, there was very little suggestion of conjunctivitis, and I had not used silver nitrate on the palpebral conjunctiva.

For a number of years I have used a rather unusual treatment instead of silver nitrate for severe conjunctivitis. It consists of 15 grains of zinc sulphate in an ounce of water after anesthetizing the eye, followed by thorough irrigation. I substituted this for the silver nitrate. Three applications cleared this case up promptly.

Dr. W. M. James, St. Louis, Mo.—Dr. Thomas has very judiciously eliminated from the discussion those conditions in which the corneal pathology is secondary to extensive intra-ocular change such as follows absolute glaucoma, long-continued uveitis, or those corneal changes due to exposure, either from lack of lid coverage or corneal sensitivity such as follows trigeminal or facial nerve lesions.

The discussion is limited to the recurrent erosions of the cornea which are traumatic, herpetic or neurotrophic in origin.

The traumatic lesions are usually caused by a glancing blow which produces relatively a superficial abrasion of the cornea with little or no penetration of the underlying stroma. The symptoms of the immediate injury are very variable. In my experience this particular type of injury is best handled by:

(1) Thorough anesthesia of the eye.

(2) The complete removal of loose or torn epithelial shreds and all foreign substances from the wound.

(3) The application of a tight, firm bandage which fixes the lids.

This point warrants some elaboration. The movement of the lids across a denuded corneal area is painful, and it interferes with the epithelization process. If satisfactory healing has occurred and the lesion erodes more or less spontaneously, the application by the physician of a firm bandage for four or five days will often allow adequate union to occur between the epithelium and the underlying tissue. The point I wish to make is that frequently the manipulation of the lids by the patient, or some heavy handed attendant, may cause a disruption of the new epithelium. Pain satisfactorily controlled by general medication eliminates the necessity of the frequent instillation of drops. Too much local meddling or treatment interferes with nature's repair process.

A large number of recurrent erosions of the cornea are associated with injury to Bowman's membrane. It has long been known, in fact since 1855, when von Graefe made the observation in discussing bullous keratitis that when necrosis or secondary infection of the corneal vesicle (which antedates the erosion) takes place a new vesicle never forms in that area. The union of epithelium to corneal stroma is much firmer than the union of epithelium to Bowman's membrane. This has been verified by von Graefe, Fuchs, Thomas and others. In other words, if healing has occurred and the epithelium is lifted away from Bowman's membrane and sloughs away, the local destruction of Bowman's membrane will permit a firmer union between the corneal stroma and epithelium. This often occurs if the erosion becomes infected and a sloughing ulcer results.

The local destruction of Bowman's membrane may be accomplished with trichloracetic acid or with a sharp curette or by cautery. The method is optional. The desired end is the local destruction of Bowman's membrane, that is, a firm, healthy tissue base forms a satisfactory base for epithelium. This step in therapy may very well be made a part of the first treatment for the patient with a nasty looking corneal abrasion.

The second group of corneal erosions due to herpes, a virus infection, may be considered. There is nothing in the gross appearance of a single herpetic erosion to differentiate it from a single traumatic erosion.

(1) Corneal sensitivity, tested by a wisp of cotton, is often lowered in herpes. In fact, the degree of loss of corneal sensitivity is a lead as to the severity of the infection. There is no appreciable loss of corneal sensitivity in traumatic erosions; the eye is hypersensitive.

(2) Staining of the lesion with methylene blue and counterstaining with fluorescein show that the herpetic erosions are surrounded by a relatively wide zone of damaged epithelium. The area of ulceration stains blue and the undermined epithelial edges of the dendritic lesion takes the green fluorescein stain for approximately a millimeter about the area.

I have found in dealing with dendritic ulcers and herpes that the use of strong tincture of iodine locally is entirely satisfactory, provided the application is thoroughly made and generously applied. The herpes virus must be destroyed. It is not destroyed by gingerly dabbing at the ulcerated area with tincture of iodine. The undermined epithelial zone and areas of infiltration must receive the iodine locally, generously and thoroughly. One or two drops of cocaine solution should immediately follow the iodine application.

Now for the neurotropic or neuropathic group of recurrent corneal erosions. The name is a screen for our ignorance of the condition. We might as well call it idiopathic erosion of the cornea. Some may be due to allergy; some may be due to local avitaminosis. If so, the effective treatment is apparent and the condition is no longer in the neuropathic group.

In several patients with recurrent erosions of the cornea which have existed not for weeks or months, but for years, satisfactory healing and relief has followed the removal of the superficial layers of the cornea. The removal of Bowman's membrane may be accomplished very simply and safely by infiltrating the corneal stroma in air. This is done by injecting air into the tissues with a 2 c. c. syringe and a fine hypodermic needle. After the corneal substance is ballooned out with air, the natural cleavage planes of the cornea are opened up by the air and the tissue may be peeled off layer by layer. Healing has been satisfactory and uneventful. The union of epithelium and stroma has been firm. The procedure is recommended only when the corneal erosions have existed for a great period of time. The visual acuity is greatly reduced by previous scarring and the patient is disabled by the corneal disease.

To summarize:

(1) A firm bandage with the minimum amount of lid manipulation will often prevent recurrent erosions.

(2) The local destruction of Bowman's membrane by trichloracetic acid, surgically or by cautery, is often essential for permanent healing.

(3) The neurotrophic group is of unknown etiology; the widespread removal of Bowman's membrane may be followed by satisfactory healing.

(4) A simple technic of removing the superficial layer of the cornea by supporting the layer with air has been offered.

Dr. Thomas (*closing*).—Protection of the cornea is essential in all types of corneal erosions.

My experience with other forms of therapy has been varied as I have used zinc sulphate, but not in this proportion. However, it was not wholly satisfactory.

Several cases have come to me in which x-ray had been used. I became a little chicken hearted about sending them back for a second try when the first proved ineffective.

FURTHER OBSERVATIONS ON THE PATHOGENESIS AND LOCALIZATION OF PULMONARY TUBERCULOSIS*

By BENJAMIN L. BROCK, M.D.†
Waverly Hills, Kentucky

In recent years our attention has been called to the significance of the role of insidious apical and acute subapical pulmonary tuberculosis in the pathogenesis of pulmonary tuberculosis. The insidious apical lesions have been described as obsolete foci, the active stage of which has passed unnoticed. On the other hand, the subapical or infraclavicular lesion is very significant so far as pathogenesis is concerned. In this paper a new concept will be discussed as it relates to the important subject of pathogenesis and localization of pulmonary tuberculosis.

Why is primary tuberculosis situated in any portion of the lung while the reinfection type of disease is usually found in the upper portion of the lung? In the absence of tuberculous disease in other parts of the lung field, why is the typical chronic nodular productive lesion situated in the extreme apex rather than in some other portion of the lung? Why is this apical focus a chronic nodular productive lesion which becomes obsolete? Why is it infrequent that an acute tuberculosis is seen in the extreme apex in the absence of disease elsewhere in the lung? Why is it a frequent finding on the other hand that acute tuberculosis is located initially in the subapical region? Since the acute subapical lesion is recognized as being very unstable, what are the factors involved in the clearing of the lesion on the one hand and destruction and spread to other parts of the lung on the other?

When tubercle bacilli are inhaled for the first time, they may be carried into a primary lobule situated anywhere in the lung field. These bacilli are treated like foreign matter, such as fine dust particles which may be inhaled into the lungs. The tissues are not hypersensitive to them, and they, like the fine dust particles, are phagocyted and carried to the nearest lymphoid tissue. If the organisms are in sufficient dosage, an anatomical tubercle is a foregone conclusion, since they are now within the closed lymphatic system and cannot be physically evacuated from the lungs as would be the case if we were dealing with organisms of reinfection. The primary tubercle develops, therefore, in any portion of the lung field, apex or base, depending upon the location of lodgment of the bacilli of first infection. Throughout the whole development of the primary complex the parenchyma of the lung itself, in many instances at least, is found to be free of tuberculosis. The closed lymphatic system is effective in most instances, therefore, in preventing the development of reinfection tuberculosis.

It has long been known that hematogenous tuberculosis confined for the most part to the lung tissues usually has a favorable prognosis. The localization of lodgment of the bacilli is similar to that of primary tuberculosis in that they remain within the interstitial tissues and do not reach the air spaces in large numbers. They remain fixed locally, therefore, and are not spread by way of the bronchial tree.

Let us now consider the possible sequence of events which take place following the inhalation of tubercle bacilli from an exogenous source into the lungs of an individual already primarily infected. Again it is not believed that the tubercle bacillus has an affinity for the upper portion of the lung where reinfection tuberculosis commonly develops and progresses for reasons peculiar to the tubercle bacillus itself or to the lung tissue in this region. Bacilli from an exogenous source must certainly reach any portion of the lung field, and where the particles inhaled are small enough they, too, are carried to the terminal divisions of the primary lobule. Shortly after reaching their destination, however, an entirely different type of reaction occurs from that described under primary infection. The bacilli are, under these conditions, not treated as a foreign body to be phagocyted and carried to lymphoid tissue situated outside the parenchyma proper.

On the other hand, a specific reaction to them occurs, since the tissues are now hypersensitive to them. The allergic reaction which follows consists of an edematous thickening of the lung tissue and the pouring out of an exudate which has a tendency to hold the bacilli within the air spaces. The bacilli, therefore, are not in a closed system, but are within a continuous open system, and they, together with their exudates, have every opportunity to be drained from the lung through the bronchial tree. Since it takes days for the anatomical tubercle to develop, it is obvious that the expulsion of the infectious exu-

---

*Read in General Clinical Session, Southern Medical Association, Thirty-Fourth Annual Meeting, Louisville, Kentucky, November 12-15, 1940.

†Waverly Hills Sanatorium, Waverly Hills, Kentucky.

dates, produced by ordinary small dosages of bacilli of exogenous origin, would be effected long before this could take place. Due to the comparative small dosage of organisms taken into the lungs in this manner it is quite probable that no clinical manifestations would be observed. These small reactions would also probably never be revealed by x-ray. However, such small reactions must occur much more frequently than is ordinarily believed. Individuals with primary tuberculosis frequently remain for long periods of time in contact with open cases of pulmonary tuberculosis and never show evidence of manifest disease. It is believed and taught that individuals who have not been previously infected with the tubercle bacillus remaining in contact with open cases of pulmonary tuberculosis for long periods of time will almost surely be primarily infected. It is estimated that 50 per cent of the population of the United States, or 65,000,000 individuals, have been primarily infected. On an average these 65,000,000 individuals will continue to inhale into their lungs tubercle bacilli from an exogenous source after the primary tubercle has been established. Yet it is estimated that only 650,000, or 1 per cent of these 65,000,000 individuals, suffer at the present moment from active adult type disease.

We have no evidence to show that the tubercle bacillus reaches the lymphatic system following the development of the primary complex. This would not indicate that the individual has developed an increased immunity to the tubercle bacillus. The fact that only 650,000 individuals in the United States have at the present time reinfection tuberculosis would indicate that the great majority of individuals who become primarily infected have already a high degree of immunity to the tubercle bacillus. Otherwise the closed lymphatic system, as already stated, would not be effective in preventing the spread of the primary lesion to the parenchyma of the lung in a large percentage of the cases. What happens then to bacilli that are inhaled into the lungs of individuals already primarily infected? Since they are not carried to lymphoid tissue which lies in the interstices of the lungs, they must remain in the air spaces, and since the lung tissue is hypersensitive to them an allergic inflammatory reaction occurs. The exudate formed is usually small, since bacilli from an exogenous source usually reach the lungs in small numbers at any one time. This exudate, together with phagocyted and free bacilli, must be expelled from the bronchial tree. Allergy plus the mechanics of the bronchial tree, therefore, must play a predominant role in the prevention of exogenous reinfection tuberculosis in the great majority of the population, and yet allergy must also play a chief role in the development of tuberculosis in those individuals who have a highly developed allergy. Allergy holds the bacilli in the open air spaces and in most instances they are expelled. Where infection is large or where allergy is highly developed as in the negro or 'teen age groups then drainage cannot be effected and retrograde reinfection occurs.

The normal movements of the lungs, and it is believed the normal function of the diaphragm is important in this regard, is conducive to the evacuation of foreign material in moderate amounts from the bronchial tree. The efficient manner in which the bronchial tree rids itself of foreign material under ordinary conditions has long been known, but due consideration has not been given it in pulmonary tuberculosis. The movement of the lung, together with the lengthening and shortening movements of the bronchial tree, is much greater in the lower portion than in the apical region. Macklin,[1] in his "Dynamic Bronchial Tree," has clearly described and demonstrated the movements of the bronchial tree during respiration. The restricted movements of the bronchial tree,

> "in the area of the human lung which lies between the root zone and the fixed wall behind and above the root region,"

have been emphasized by this author. It is clearly believed that small exudative processes resulting from ordinary exogenous reinfection are insignificant from a clinical standpoint at least, since they are effectively drained from the bronchial tree. This certainly holds true so far as the base of the lung is concerned. This bronchial mechanism may truly be just as effective in protecting the individual from reinfection of exogenous origin as the lymphatic system is effective in preventing reinfection from primary foci in the lung. It would appear that this would apply particularly to exogenous reinfection in the base of the lung, and yet the bronchial tree must also be very effective in preventing spread of disease where active open tuberculosis already is present in the upper part of the lung. Tubercle bacilli must constantly invade the base of the lung in such individuals, but tuberculosis certainly does not develop as a rule following such an invasion in this region.

On the other hand, there may be a close relationship between exogenous reinfection and apical tuberculosis. It is quite probable that the

typical chronic nodular productive apical lesions in the absence of tuberculosis elsewhere in the lung field might well be explained on the basis of an exogenous reinfection. Due to the very limited movement of the lung in the extreme apex, it is believed that bacilli might remain in contact with the lung tissue long enough for the development of tubercle in this region. The lesion rarely becomes acute enough to produce symptoms or to show x-ray evidence of an acute lesion, since the usual infecting dose of organisms from an exogenous source at any one time must be small. The small amount of exudate is formed in the alveoli and the foci which develop are therefore terminal foci. There is usually never any blockages of bronchioles by the exudate and the lesions remain terminal and become obsolete.

Based on the fact that temporary partial blockage may occur in a main stem bronchiole from which many terminal bronchioles branch, it seems likely that bacilli in large numbers coming from an exogenous source or from a primary focus rupturing into a bronchus might set up a retrograde reinfection process and account for the development of the acute subapical lesions more frequently than from other possible sources. As already stated, there is distinctly less movement of the upper part of the lung during respiration than there is in the base. For this reason, bacilli may take hold in this region more frequently than in the base. The size and physical characteristics of the material containing the bacilli of endogenous origin might be a factor in preventing them from being carried initially to the terminal lobules themselves. Due to the comparative inability of the bronchioles in the upper third of the lung to rid themselves of infectious exudates in unusual amounts, and particularly following loss of contractile power of the lung following the allergic reaction, progressive disease usually results. This might account for the frequency of acute subapical lesions.

Acute destructive reinfection tuberculosis occurring initially in the base of the lung must become established in similar manner following unusually large allergic reactions. The base of the lung may be very effective, however, under adverse conditions in expelling exudates following serious bronchogenic spreads. We have all seen such spreads to the base from an active lesion in the upper third of the lung. Such basal lesions may often clear while the original upper lobe lesion remains unchanged.

The acute allergic pneumonic process is unstable, therefore, and is potentially a progressive and destructive tuberculosis for the reasons given above.

The relatively high degree of allergic response to reinfection in the 'teen age group and particularly in the negro might explain the progressive nature of the disease in these individuals, since the bronchial tree under such conditions would be unable to initiate an adequate drainage of the exudates from the lungs.

Some of the conclusions reached in this paper are based on a five-year study of one hundred and fifty patients with extensive pulmonary tuberculosis confined chiefly to the upper half of the lungs, who have been treated at the Waverly Hills Sanatorium by simply elevating the foot of their beds.[2 3 4]

Increase in the intra-abdominal pressure which follows this procedure results in a rise of the diaphragm and a more evenly distributed expansion and relaxation of the lungs during respiration. The upper third of the lung now becomes more mobile and functions similarly to the rest of the lung with more vigorous lengthening and shortening movements of the bronchial tree. This results in good drainage in this otherwise less mobile apex. Of those patients complaining of difficult expectoration prior to the raising of the foot of the bed, ease of expectoration followed very shortly in 85 per cent of the cases. Other symptoms such as cough, failure to relax, and shortness of breath were equally relieved following proper drainage of this tenacious exudate from the bronchial tree. From the standpoint of the x-ray, general improvement occurred in 65 per cent of the cases, while 34 per cent of the patients with cavity closed them.

Retention of infectious exudate in main stem bronchioles in the upper third of the lung, due to comparative lack of mobility of the lung in this region, is directly responsible not only for the prevalence of tuberculosis in this region, but for its progression and chronicity.

SUMMARY

(1) Tubercle bacilli of first infection are carried by the phagocytes to a closed lymphatic system, and if in sufficient numbers tubercle is a foregone conclusion. The location of primary anatomical tubercle is therefore dependent upon the location of lodgment of the bacilli.

(2) Tubercle bacilli of reinfection, together

with their exudates, remain temporarily within the open air system and usually have every opportunity to be drained from the bronchial tree before reinfection occurs.

(3) The normal bronchial mechanism may truly be as effective in protecting the individual from reinfection of exogenous origin as the lymphatic system is effective in preventing reinfection from primary foci in the lung.

(4) Typical chronic nodular productive apical lesions, in the absence of tuberculosis elsewhere in the lung field, might well be explained on the basis of an exogenous reinfection.

(5) Retention of infectious exudate in main stem bronchioles in the upper third of the lung, due to comparative lack of mobility of the lung in this region, is directly responsible not only for the prevalence of tuberculosis in this region but for its progression and chronicity.

BIBLIOGRAPHY

1. Macklin, C. C.: The Dynamic Bronchial Tree. Amer. Rev. Tb., **25**:393, 1932.
2. Brock, Benjamin L.; and Woodson, T. A.: Postural Treatment of Pulmonary Tuberculosis. Ky. Med. Jour., **36**:343-346 (Aug.) 1938.
3. Brock, Benjamin L.; and Woodson, T. A.: Elevation of the Foot of the Bed in the Treatment of Pulmonary Tuberculosis. Jour. Amer. Acad. Tb. Physicians (Aug.) 1939.
4. Brock, Benjamin L.: Pathogenesis and Localization of Pulmonary Tuberculosis. Amer. Rev. Tb., **42**:755 (Dec.) 1940.

TEN YEARS IN MATERNITY AND INFANCY WORK IN NORTH CAROLINA*

By GEORGE M. COOPER, M.D.†
Raleigh, North Carolina

The scope of this paper might just as easily extend over a period of twenty-five years, as the writer has been a staff officer of the State Board of Health for more than that time and concerned most of the period personally, professionally and officially with questions of maternal and child health. The selection of a period of ten years, however, answers the purpose very well. Vital statistics for this period are more or less accurate and ten years should be a sufficient length of time to undertake to cover in a paper of this character.

The years selected, 1930 to 1939, inclusive, cover the worst years of the depression as well as the recent years of world-wide terror affecting the people in all civilized countries. It includes the enactment of Social Security legislation as we now know it with the material Federal aid now being extended to the states through such work as the maternal and child health services, the crippled children's work, as well as the general public health administration work in all its phases.

In some respects our position in North Carolina in this field presents many puzzling aspects. Some can be explained and some cannot. In order to place emphasis right in the beginning of this discussion that progress along all public health lines and particularly in the maternal and child health field is a slow and tedious procedure, I have prepared a summary set forth in a few tables which should be considered in connection with the facts and conclusions brought out in this discussion. There are four of these tables which embrace the following classifications: *Table 1,* total number of births and the rate from 1930 to 1939, inclusive, in the State of North Carolina; *Table 2,* total number maternal deaths, also by race and rate per thousand live births for the same period; *Table 3,* total number of deaths under one year of age and by race with rates per thousand live births; *Table 4,* deaths from diarrhea and enteritis under two years of age for the period mentioned above.

I am making no comparisons in detail with other states. All of us have available statistics from other states, but each one of us knows conditions in our own state better than we do

Table 1

Total Number Births and Rate, 1930-1939

Year	Indian	Total		White		Colored	
		No.	Rate	No.	Rate	No.	Rate
1930	521	76,717	24.1	53,515	23.9	22,681	24.6
1931	577	74,743	23.2	51,806	22.8	22,360	23.5
1932	623	77,880	24.0	53,655	23.4	23,602	25.2
1933	567	75,322	23.0	51,490	22.3	23,265	24.1
1934	686	79,556	24.1	54,438	23.3	24,432	25.5
1935	755	79,596	23.3	54,199	22.4	24,642	25.1
1936	695	76,321	22.1	52,408	21.5	23,218	22.9
1937	809	79,244	22.7	53,857	21.9	24,578	24.6
1938	787	79,903	22.7	54,469	21.9	24,647	24.0
1939		80,421*	22.8*	54,823*	22.0*	25,598†	24.6*

*Provisional.
†Indians included.

*Read in Section on Public Health, Southern Medical Association, Thirty-Fourth Annual Meeting, Louisville, Kentucky, November 12-15, 1940.

†Director, Maternal and Child Health, North Carolina State Board of Health, Raleigh.

anywhere else. Every individual reading or listening to this paper is, therefore, free to draw his or her own conclusions and make his or her own comparisons. There are a few notations, however, which should be considered somewhat in the nature of exceptions to the statement just made. For example, taking 1938 as the year for which we have the latest complete figures, it will be noted that in North Carolina the birth rate of 22.9 was higher than that recorded in any other state in the Union with four exceptions, namely: Utah, New Mexico, Mississippi and Arizona. In all the years since the registration area included all of the United States, the birth rate in North Carolina has been one of the four highest in the Union. Just why is one of the puzzles. The ratio of negroes in the population is not so large as that of several other Southern states. The State has fewer foreign born among its people than any other state in the Union. In the same year, 1938, the infant death rate was slightly over 68, exceeded that year by only three other states in the Union. Those were South Carolina, and again Arizona and New Mexico. Again in 1938, of approximately eighty thousand births reported, about twenty-one thousand, or 26 per cent of the women, were attended solely by midwives. There are only about six other states in the nation that have a higher per cent of midwife deliveries. Of the deliveries in the State, 10 per cent, or about 4,500, were white women, and 63 per cent, or a little under 16,000, were negro women who were attended by midwives. This is a much better record, however, than that recorded at the beginning of the ten-year period, in which about 17 per cent of white women and about 80 per cent of negro women depended upon midwives.

In 1917, when the first midwife registration was required by law, about 9,000 midwives were registered. The number has been constantly reduced until today fewer than 3,000 midwives are at work in the State. Their qualifications in many respects have been improved, a Wassermann test is required annually of each one of these midwives and a woman found to have a positive reaction is not allowed to work until sufficient medical treatment has been provided to make it safe for her again to resume her duties.

It need hardly be stated here that it is a well-

Table 2

Total Number Maternal Deaths also by Race and Rate (per 1,000 Live Births) in North Carolina, 1930-1939

Year	Total	Rate	White	Rate	Colored	Rate
1930	640	8.4	363	6.7	277	12.2
1931	640	8.6	359	6.9	281	12.6
1932	560	7.2	310	5.8	250	10.3
1933	535	7.1	319	6.2	216	9.3
1934	606	7.6	363	6.7	243	9.7
1935	554	7.0	316	5.8	238	9.5
1936	532	7.0	309	5.9	223	9.6
1937	445	5.6	232	4.3	213	8.4
1938	450	5.6	240	4.5	210	8.4
1939	394	4.9*	222	4.0*	172	6.7*

*Provisional.

Table 3

Total Number Deaths Under One Year of Age and by Race with Rates per 1,000 Live Births in North Carolina, 1930-1939

Year	Total	Rate	White	Rate	Colored	Rate
1930	6,021	78.4	3,583	67.0	2,438	105.0
1931	5,459	73.0	3,109	60.0	2,350	102.4
1932	5,173	66.4	3,064	57.1	2,109	87.0
1933	4,974	66.0	2,824	54.0	2,150	90.2
1934	6,196	77.9	3,657	67.1	2,539	101.0
1935	5,407	67.9	3,191	58.9	2,216	87.3
1936	5,221	68.4	3,123	59.6	2,098	87.7
1937	5,164	65.2	3,017	56.0	2,147	84.6
1938	5,461	68.3	3,244	59.6	2,217	87.2
1939	4,670	58.1*	2,722	49.6*	1,948	76.1*

*Provisional.

Table 4

Diarrhea and Enteritis (Under Two Years of Age) in North Carolina, 1930-1939

Year	Total		White		Colored	
	Number	Rate	Number	Rate	Number	Rate
1930	1,112	35.0	638	28.5	474	50.7
1931	837	26.0	501	22.1	336	35.4
1932	647	19.9	370	16.2	277	29.0
1933	804	24.5	463	20.0	341	35.3
1934	1,001	30.3	555	23.8	446	45.8
1935	852	24.9	524	21.7	328	32.8
1936	842	24.2	519	21.3	323	31.8
1937	860	24.6	504	20.5	356	34.5
1938	1,030	29.2	590	23.8	440	42.2
1939	666	18.8*	378	15.2*	288	27.6*

*Provisional.

understood fact that where the birth rate is high, the infant death rate will be higher than otherwise. Another thing which has been brought out in many studies, notably by Dr. Frederick Holden, for many years professor of obstetrics and gynecology at the New York University Medical School, is that the infant death rate when babies are born at intervals of one year is fully 30 per cent or more higher than where the interval is two years apart. Naturally where the births come too close together, prematurity is a cause of many more infant deaths.

The record of our State is better in the matter of maternal deaths than it is in infant deaths. It will be noted by reference to *Table 2* that the maternal death rate in this ten-year period has been cut almost in half. Another specially significant point is that the negro maternal death rate in 1939 was down to the same point as the white rate in the year 1930. Both white and negro rates have been cut almost exactly in half. In justice to our State, it may be said that the infant death rate for 1939, which we cannot analyze fully at this time, was lower by ten points than has been recorded before. The rates for 1940 will probably run even a little lower. At the same time other states have made as much progress in reducing their rates as we have, leaving us somewhere in the same relative position we have occupied for several years.

Another point I wish to emphasize is that it will be noted that the birth rate has varied but little in the ten-year period. This is true of both white and colored races, the colored rate being exactly the same in 1939 as it was in 1930 and the white rate being only about one point lower. Notwithstanding our high comparative birth rate, our high infant death rate, the general death rate in North Carolina per thousand population has for all these years ranked lower than that of about forty other states. To be exact, in 1938, only nine other states recorded a general death rate lower than the State of North Carolina.

According to data classified by the *Journal of the American Medical Association*, our State has two hospital beds per thousand population and shares forty-third rank with Tennessee in this respect. According to tabulations by the same authority, of all hospitals, including general, nervous and mental, the State of New York ranks first with 14.01 hospital beds per each thousand inhabitants. The United States average is about twice that of North Carolina. Also, our State has no hospital whatsoever in 39 of its one hundred counties. Finally, our State ranked 46 among all the states in 1936 with one practicing physician for each 1,346 inhabitants. In Durham County there are 261 inhabitants to each physician and in Tyrrell County at the foot of the list there is one physician for its 5,164 inhabitants.

The foregoing is simply a presentation of facts which represent some of the problems with which we have had to deal during these years. The principal cause of maternal deaths, as elsewhere, may be said to be the toxemias of pregnancy in each of these years which accounted for more of the puerperal deaths than any other single cause. The second largest number of deaths recorded were caused by puerperal septicemia, and the third from puerperal hemorrhage. The toxemias of pregnancy accounted for about 30 per cent of all maternal deaths.

The causes of infant deaths as in previous years were about the same. In 1938, for which the figures as stated above have been tabulated, five principal causes of infant mortality accounted for 70 per cent of all infant deaths under one year of age. These causes were premature birth, which accounted for 1,502 deaths; diarrhea and enteritis, 847; the pneumonias, 675; sudden death with cause not specified, 470; and congenital malformation, 334.

I have always held to the opinion that the infant death rate in our State could be materially reduced and reduced permanently only through the extension of more and better obstetric care for the prenatal period on through to a satisfactory postpartum.

We have been asked many times for an expression as to a comparison of the maternal mortality between midwife and physician deliveries. This question can never be answered for the simple reason that when the patient who is being handled by the midwife gets in an extreme condition, efforts are made to procure a physician and many times he is only able to get there in time to sign the death certificate. The death then is charged up as a physician's loss and not to the midwife. It is only a common sense conclusion to feel that with competent, scientific and careful medical care from the beginning of pregnancy until an uneventful postpartum period is reached, that the infants as well as the mothers will have a much better opportunity to live. In this connection the figures for 1938 recorded the further fact that 24 per cent of all our infant deaths occurred during the first day of life and

38 per cent within the first week. Naturally, only better obstetric care could save these deaths which would make all the difference in the world in our rates.

I was much impressed some time ago with the statement attributed to Dr. Arthur Compton that there have been more important changes affecting all the people of the world in the last fifty years than there were all together in the previous two thousand years. Dr. W. C. Davison, Dean of the Duke University School of Medicine and Professor of Pediatrics there and author of one of the best books on pediatrics I have ever seen, remarked that in so far as the everyday practice of medicine was concerned, there have been more vital changes made in ordinary medical practice in the last two years than have been made in the previous twenty. This leads to a further discussion of the situation of pediatrics in our State at this time, and I am permitted to quote from Dr. Davison's ten-year report of the pediatric department of Duke University Medical School to the President of that University recently made in a paragraph on the "Future of Pediatrics:"

"Twenty years ago one-quarter of all deaths were in children, but today the ratio has fallen to one-eighth, a reduction of 50 per cent. That this decrease is not due to the falling birth rate is indicated by the fact that during this same period the ratio of children to the total population fell from one-third to one-quarter, a 25 per cent reduction. In other words, the decrease in the pediatric death rate is twice as great as the fall of the birth rate. The need for the hospitalization of ill children should eventually decrease, as diphtheria, whooping cough, dysentery and typhoid fever become rarities, as pneumonia and meningitis are treated at home with sulfapyridine or other drugs, as congenital syphilis decreases through the expansion of the program for treating adults and as nutritional problems are eradicated by the simplification of infant feeding.

"Seventy-five per cent of the deaths among children are preventable. * * *

"The need for pediatric hospital care has been or will be reduced, but the importance of preventive pediatrics has been accentuated. The pediatric dispensary will grow because of the increasing number of mothers who are bringing their children for advice and preventive measures.

"Although pediatrists always will be needed in practice, prevention and teaching, because the problems of children differ from those of adults, the bulk of the medical care of children will be in the hands of general practitioners. Our problem, therefore, has changed; ten years ago it consisted of clinical pediatric instruction for many medical students, who would have little use for it in other specialties, and the provision of post-graduate training for future pediatrists. Now the latter are decreasing, but a greater need has arisen—greater stress on preventive measures, the better pediatric training of future general practitioners, and short intensive pediatric courses for physicians who have been in general practice for several years."

In a letter to Dr. Davison from Dr. Martha M. Eliot, Assistant Chief of the United States Children's Bureau, the statement was backed up with statistics that in an enumeration of eight important causes of deaths of children under 15 years of age in the last ten years there had been a reduction in the number of deaths from all of the eight causes ranging from infections and parasitic diseases to accidents, except premature births from which there had been a steadily increasing number of deaths. Prematurity, resulting as it does frequently in a majority of cases from the toxemias of pregnancy, represents one of our biggest problems. This is inextricably tied in with obstetric practice.

MEETING THE NEEDS

In an effort to deal with the situation described, different as stated in the beginning of this paper from conditions existing in most other states, we have slowly and gradually worked out a plan of procedure that is little different from methods found successful elsewhere in most particulars. We may outline our plan as follows:

(1) To extend and stress our education methods in every conceivable manner.

(2) Prenatal and well baby clinics have been established in more than half our counties. These clinics received last year more than thirty thousand visits from pregnant women and more than twenty-six thousand visits from infants. About two hundred practicing physicians in the State contributed their services on a part-time basis in addition to the health officers and the health department nurses. One thousand five hundred and ninety-six pregnant women were found to have signs and symptoms of toxemia of pregnancy and six hundred and eighty-three mothers were subsequently hospitalized from this group. A Wassermann test was made on every woman at her first visit and about 13 per cent of all of them were found to have positive reactions. Most of the babies were immunized against diphtheria and about fifty thousand pieces of literature were placed in the hands of these families. This work was purely for indigent families. Most of the women were those who looked to midwives for delivery and none of the families had any regular family physician.

(3) As the hazards for maternal mortality as pointed out are much greater in mothers who have babies about once a year and the same

hazard therefore extends to the babies of such mothers, a scientific effort has been made to reduce the number of repeated pregnancies in mothers who are making bad medical risks and to extend the spacing of pregnancies from one year to two or three years at least among the class of women dealt with.

(4) Every effort is being made gradually to reduce the number of midwives engaged in work to the point of eliminating them entirely as we have already practically done in two of our large counties and to provide in their stead either a system of hospital deliveries as carried out in one of our counties for indigent cases, or a system of bedside deliveries by competent physicians as successfully instituted in another of our counties. A brief description of these two plans which have been successfully launched and carried on now for some years should be of interest here.

In Wilmington and New Hanover County midwives have been largely eliminated. For several years, prenatal instruction to expectant mothers in nurse conferences attended when needed by competent obstetricians has been provided. These women have been admitted to an endowed hospital in that county and delivered by the interns there. When the hospital is crowded and beds are scarce, the mothers are taken home with their babies sometimes in two or three days, accompanied by the health department nurse, who makes visits every day for a period of ten days. It has reduced both the maternal and infant mortality materially in that city and county.

The other plan is in Charlotte in Mecklenburg County and is a part of the Duke Medical School outpatient department working in combination with the health department of the City of Charlotte and under the specific direction of the health department, financed by several agencies, including the Maternal and Child Health Division of the State Board of Health. The plan there is for a resident physician supplied by the Duke Medical School to serve for a three months' period and to direct the services of two senior medical students working on a rotation basis of two weeks each. Cars and every equipment are provided these students. Bedrooms are equipped in the City Health Department offices and the students are on call day and night. Ten years ago Charlotte had about ninety-two midwives registered and working. Today the number has been reduced to less than a half dozen. The system in brief is when the call comes, day or night, one of the students answers. He makes the delivery in the home in the surroundings he finds, carrying sterilized equipment, of course. If in his judgment the situation is abnormal and beyond his power to deal with, he calls the resident physician. He in turn if he deems it necessary orders the woman taken to one of the hospitals, and the head of the outpatient department or one of the specialists in obstetrics in Charlotte who is on the consultant staff is called and the woman given every attention necessary. It also has greatly reduced the maternal and infant death rate in this class of the population. Hospital deliveries there also have been greatly increased.

The first of these plans could not be put into effect anywhere unless there were hospital facilities financially able to carry the load, but the second plan, that followed in Charlotte, is practical and within financial reach.

A third plan we have worked out in conjunction with local authorities is in Moore County, where a nurse-midwife supervises in detail the work of every midwife. Maternal mortality in that county, although it includes a large hospital, has been reduced almost to nothing.

A fourth plan is our demonstration county of Northampton, aided by funds from the Children's Bureau. Strict midwife supervision is carried out, delivery of mildly abnormal cases is provided in the homes by employing physicians when needed, and hospital service is available. This plan is proving highly successful, although expensive.

(5) The most recent plan we have been able to work out, a new plan we have just inaugurated in cooperation with the Children's Bureau, which agency largely finances the enterprise, is a cooperative arrangement between the State Board of Health, the Public Health School at the University of North Carolina and Duke Hospital and the Medical School there. This arrangement calls for the employment of a specialist in pediatrics and one in obstetrics. Their duties are divided as follows: during the fall months physicians assisting us in our clinics or other general practitioners largely engaged in work for women and children are invited in groups of about five to attend an intensive postgraduate course in the Duke Hospital and Medical School, arranged there by the faculty in pediatrics and obstetrics. This course extends for about five days, the time being divided between intensive pediatric instruction on a personal basis to the group by the pediatrician and by the ob-

stetrican; clinical facilities in the Duke Hospital are available for teaching purposes. These men also lecture to the seniors in the regular medical school at periodic intervals. Room and meals are provided for the physicians who accept this invitation and the clinical facilities in pediatrics and obstetrics not only in the Duke Hospital but other hospitals in Durham and the city health department work are available for their observation free of cost to them. In the middle winter quarter both of these men are accepted as full professors in the University of North Carolina School of Public Health and teach an intensive course in obstetrics and pediatrics, respectively, during the quarter in that school. The arrangement offers material advantages to the men taking training as health officers for special information in this field. It is expected that much good will result from this course when such men become health officers later on.

A third phase of this program is to enable the pediatrician and obstetrician to conduct symposia before local medical societies in a sort of brief postgraduate course to such groups. This is expected to be one of the most important features of the program. In this way we hope eventually to reach into every community in the State and to arouse a state-wide consciousness among physicians and the public generally in an effort materially to reduce infant and maternal mortality in the State of North Carolina.

DISCUSSION (*Abstract*)

Dr. R. W. Ball, Columbia, S. C.—A tabulation of the successes or failures of a single year is apt to carry with it the erroneous impression often arising from the study of a small sample. But when that record dates back over the period of a full decade then one may draw fairly reliable conclusions. As was stated in Dr. Cooper's paper, that decade includes some of the worst, as well as the best, years of public health. It includes those years of depression in which public health, like many other fields of endeavor, became moribund, then to be revivified and rejuvenated by the passage of the Social Security Bill; that bill which has subsequently made possible tremendous strides in programs for the betterment of the health and welfare of our people. Throughout this period North Carolina, according to the paper just presented, has shown a fairly uniform birth rate and a consistent decline in its maternal death rate, its infant death rate, and deaths from diarrhea and enteritis. These three have shown a reduction during that period of one-half, one-third and one-half, respectively. This is indeed a record of which any state might be justly proud.

The problems of North Carolina are akin to those of her sister state, South Carolina, directly comparable to those of the Southern states, in many respects to those of all states. The various means by which the needs are being met are means with which you are all familiar. There is one theme, however, which runs through the program. This is a keynote which Dr. Cooper struck when he advocated "More and better obstetric care for the prenatal period on through to a satisfactory postpartum." To use the stereotyped phrase, "This cannot be over-emphasized," particularly for the prenatal period, for it is during the antenatal period that the causes of the majority of our maternal deaths have their origin. Adequate care during this period should reduce to a minimum the hazard of delivery, regardless of whom the accoucheur may be.

In many states, especially in the South, negro midwives are frequently blamed for the high maternal mortality. While to a certain extent this may be true, it is largely more of an assumption than an established fact. For example, in South Carolina, a state where midwives deliver 45 per cent of all obstetrical cases, our midwife deliveries show a relatively low maternal mortality. In South Carolina, a five-year study of maternal mortality has been made covering the years 1935 to 1939, inclusive. Personal investigation of all the maternal deaths during this five-year period has shown consistently that only about 14 per cent of the maternal deaths occurred when midwives were the sole attendants at delivery and about 10 per cent of these deaths occurred in midwife cases relieved by physicians. Also, in this study it was found that the majority of maternal deaths occurred among women who had had no prenatal care, the lack of prenatal care among the fatal cases ranging from 87 per cent in 1935 to 53 per cent in 1939. In South Carolina, all midwives are required to place their patients under medical supervision during the prenatal period, which fact, the discussant is convinced, contributes largely to the low maternal mortality among our midwife deliveries. Further reference to our five-year study reveals that, of our maternal deaths in 1939, at least 60 per cent resulted from definitely preventable prenatal causes.

For the most part, our midwife cases attend the regular prenatal clinics organized under the maternal and child health program, which are conducted by local general practitioners. This clinic program was started in a few counties in South Carolina in May, 1936, and by 1939 this type of service was and is still being offered in every county in the State.

However, it is not simply more obstetric care, but early and better care which will eventually and inevitably lessen the hazard of childbearing. Whether the additional services other than prenatal care be through hospitalization, bedside deliveries by physicians, the employment of nurse midwives, postgraduate education in obstetrics for professional groups, or through various other means, the raising of standards and the improvement of obstetrical service is a prerequisite, for it is quality rather than quantity, not just how much is done but when and how well, that will determine the final outcome.

Dr. J. H. M. Knox, Baltimore, Md.—More lives could be saved, of course, if we could save premature babies and prevent neonatal deaths than in any other field of activity.

The suggestions of means by which the result that Dr. Cooper is after can be attained, which has been signally accomplished in North Carolina, are pertinent in all localities. They vary in their particulars somewhat, according to the needs and facilities in each community, but all have the one end in view. This may be

brought about through instructed midwives, by a nurse-midwife or physician, selecting those ordinary midwives who are conscientious and clean and can recognize danger symptoms and know where to call for help, or by prompt hospitalization or it may be through supplying nursing delivery care to doctors and so on throughout the whole gamut: all these methods are means to one and the same end, the saving of mothers and babies' lives.

No one in this country has led the procession towards this goal which we are all striving to reach more efficiently, conscientiously and successfully than has Dr. Cooper.

RESULTS OF ABDOMINAL STABILIZATIONS*

By GEORGE O. EATON, M.D.
Baltimore, Maryland

This presentation consists of a report of our experience with the Lowman abdominal stabilization operation, particularly in regard to the end results consequent to operation.

In June, 1932, Dr. Lowman presented to the American Orthopedic Association at its annual meeting in Toronto an operation to stabilize the abdominal wall in cases of polio, in which one or more abdominal wall muscles were weakened or paralyzed. He believed that by this operation

"the recapture of lost power in the presence of partial paralysis of the abdominal muscles was possible and practical. Second, that decided improvement in stabilization of trunk on pelvis was obtainable. Thirdly, that the procedure had definite corrective and preventive possibilities due to the relationship between abdominal paralysis and paralytic scoliosis."

Since 1932 we, the Staff of the Children's Hospital School in Baltimore, have done twenty-four abdominal stabilizations, of which three were done less than one year ago and so are not reported. Of the remaining twenty-one cases, we have recent check-ups on seventeen cases. The findings are as follows:

Twenty-five per cent of the cases showed an increase in muscle power under the fascia, both in cases done soon after polio and in cases done years later.

Fifteen per cent showed no change.

Sixty per cent showed a decrease in muscle power under fascia.

Sixty-five per cent of the cases showed increased power of the laterals, meaning the quadratus, the posterior fibers of the external and internal obliques, and the latissimus dorsi.

Fifty-six per cent of the cases showed increased power of muscles other than those reinforced; 12 per cent showed no change; 32 per cent showed a decrease.

The fascial reinforcement bands which have been transplanted for an average of five years were considered to be too taut in four cases; relaxed or weak in two cases. All others were firm, that is, under mild tension with the patient in a prone position.

Now as to the spinal deformities, we have classified them under three headings: kyphosis, lordosis, and scoliosis.

In the four cases in which the abdominal stabilization operation was done during convalescence, that is, before the patient was allowed up after the acute attack, these four patients were all developing a scoliosis. Its progress was arrested and no further curvature developed after operation.

Of the remaining cases, two were rapidly developing a scoliosis years after the attack of polio. In these patients the progress of the curve was arrested.

Of the remainder, nine cases showed no change in scoliosis subsequent to operation. One case, however, showed a slight increase in the curve.

Only one case showed the deformity of increased lordosis before operation, and this deformity was decreased at the time of the later check-up.

Eight cases showed a kyphosis before operation, with or without scoliosis. Four of these showed an increased kyphosis at the later check-up; all of them in adolescence at the time of operation. The other four showed no change in the degree of kyphosis.

Marked improvement in gait following operation was noted in 50 per cent of the cases which had been ambulatory before operation. There was no improvement in gait in the remaining 50 per cent.

The estimate of improvement in sitting ability is based entirely on the patient's statement. The improvement is, of course, due to increased lateral stability of the trunk on the pelvis. Again, 50 per cent of the patients showed marked improvement in sitting posture or sitting ability. The remaining 50 per cent showed no change in this respect.

Lastly, in regard to improvement in general

---

*Read in Section on Bone and Joint Surgery, Southern Medical Association, Thirty-Fourth Annual Meeting, Louisville, Kentucky, November 12-15, 1940.

physical ability, here again the estimate is based on the patient's comparison of what he was able to do before operation and what he is able to do now, at an average elapsed time of five years after operation. They were questioned on endurance, activities, lifting ability and tendency to fatigue. Seventy-two per cent of the cases believed they had benefited in this respect by the operation; several of them were quite enthusiastic about their improvement. Eighteen per cent noted no change in their general physical ability, and 10 per cent felt there had been a slight to moderate improvement. No patient felt that he was worse off than before operation.

CONCLUSION

(1) The fascial strips, after an average elapsed time of five years, are usually firm and strong and perhaps hypertrophied.

(2) Recapture of lost power in partially paralyzed abdominal wall muscles has occurred in only 25 per cent of the cases in this small series. In the cases operated upon during recumbency, following the onset of polio, the same percentage held true.

(3) Fifty per cent of the cases showed marked improvement in stabilization of the trunk on the pelvis.

(4) In the presence of a developing scoliosis the operation appeared to be very effective in arresting the progress of the deformity.

(5) In the presence of a kyphosis, the fascial reinforcement tends to increase the kyphosis, particularly if the child is growing rapidly. In two cases it has been necessary to divide the fascial band on this account.

(6) The most striking benefit has been the patient's improvement in general physical well being; activities have been broadened, endurance increased, and there is a lessened tendency to fatigue.

DISCUSSION (*Abstract*)

Dr. Charles E. Irwin, Warm Springs, Ga.—The Lowman fascial transplant and similar operations based upon this principle are valuable procedures if we first recognize the limitations of the results which may be obtained.

My experience with this procedure has not been so broad as that of Dr. Eaton and his associates. This inexperience is not due to the lack of possible cases upon which the operation could have been performed, but to disappointment that we did not accomplish all that we had hoped for in the few cases in which this procedure was employed.

Our experience has been based upon five abdominal transplants, three transplants about the upper back, and observation of four patients upon whom abdominal transplants had been done elsewhere who later came under our care. Limited beneficial results were obtained in practically all the cases. For example, from a general physical point of view, the endurance of these patients was increased, they gained in independence in their limited sphere, they felt more stable when sitting, and were better able to shift their positions while in a chair or in bed. In two cases before the operation it was almost impossible for the individuals to turn over in bed or to lift themselves from their chairs to the bed or from their chairs to the toilet without help, and these very practical accomplishments could be performed without assistance after the transplants were done. Physiologically the patients were improved because the transplant acts as a splint against which the diaphragm can exert the necessary force to increase intra-abdominal and intrathoracic pressure. The patients could better evacuate the bowel and the functions of coughing and sneezing returned. In two cases with severe abdominal weakness in which crutches and braces were necessary for weight bearing, it was practically impossible to elevate either side of the pelvis sufficiently to bring the extremity forward to take a step. The upper extremities and thoracic cage simply pulled away and the pelvis and lower extremities were left lagging behind. The transplants furnished the necessary link through which sufficient lifting force could be transmitted to the pelvis and it could be elevated enough to allow the extremity on that side to be brought forward. Due to extreme weakness in other parts of the body, however, both of these individuals at the present time spend most of their time in wheel chairs and their walking cannot be classified as practical.

Those cases in our hospital in which a transplant was done for the arrest of scoliosis and those cases which had had a similar operation elsewhere and later came under our observation, were not successful. It is entirely possible that we did not make the proper choice of our cases or that there was some fault in technic as to where the transplant was placed. We, however, came to the conclusion that our results were not satisfactory for the following reasons:

A brief review of the physiology of the spine shows that the segment to which the ribs are attached is the most rigid or inflexible part of the spinal column. The flexibility and the arc of motion through which it moves increase as we proceed distally, whether upward to the head or down to and including the pelvis. That is, each successive segment of the spine moves through a wider arc of motion as we proceed down to and including the pelvis, the sacrum and pelvis being capable of the greatest mobility and therefore instability. This is particularly true if there is weakness or imbalance in the muscles that run from the pelvis to the femora. Furthermore, scoliosis in addition to the lateral curve involves rotation and collapse. The force necessary to correct this type of curve involves traction, derotation, and angulation. Support necessary to hold a spine in a position that has been corrected in this manner, whether it be surgical or in the form of apparatus, must have a mechanical principle similar to that of a rigid prop or support. This principle, of course, is exactly the reverse of the mechanics of a guy wire. A guy wire and a fascial transplant work upon essentially the same principle. In two cases in which abdominal transplants

had been done previously Risser jackets were applied for the purpose of improving the curves which had progressed. In both cases it was necessary to divide the fascial bands before the desired amount of correction could be obtained. This was interpreted to mean that at least in these two cases the transplants were holding the spine in its collapsed position.

The fact that idiopathic scoliosis tends to progress in the presence of normal musculature rating both in back and abdomen makes it seem hardly possible that fascial strips could be so placed that they would prevent progression of a paralytic curve.

In our hands the value of this procedure is increased if we reverse our objective or reverse the part to be supported. That is, our results are more satisfactory if we perform these transplants with the idea of keeping the pelvis supported in proper relation to the spine and do not attempt to support the spine in proper relation to the pelvis. As an example, lordosis is brought about by forward tilting of the pelvis. The lumbar curve is secondary to the pelvic deformity. Therefore, it is mechanically sound to maintain the front of the pelvis in an elevated position by attaching it to the rib cage with fascia. Of course, care must be taken that no flexion contractures are present below the pelvic level and that the back muscles have been thoroughly stretched out before the procedure is performed. Lateral deviations of the pelvis in which the lumbar curve is secondary to the pelvic obliquity can likewise be improved by supporting the low side of the pelvis with a piece of fascia attached to the rib cage above. Here, again, we must be sure there are no abduction contractures below the pelvic level on the low side.

In cases of kyphosis due to posterior shoulder girdle weakness fascial transplants are useful, but these are placed at right angles to the vertical axis of the spinal column. The transplant passes from the scapula to the spine. This procedure has been performed in two cases, one with unilateral rhomboid and lower trapezius weakness and the other with bilateral rhomboid and lower trapezius weakness. The kyphosis was improved in both cases.

No doubt there are some cases of paralytic scoliosis which might be arrested by fascial transplants but I feel there are an equal or greater number which progress in spite of the operation.

While we have familiarized ourselves with the results of this operation we do not feel that its limited achievements always justify the procedure.

Dr. Lenox D. Baker, Durham, N. C.—When the lower quadrants are being reinforced, is the fascia transplanted as a free transplant, or left attached to the fascia lata muscle? If the latter, does Dr. Eaton feel that the fascia lata muscle is of assistance in actively reinforcing the lower quadrants?

Dr. Eaton (closing).—I am more or less in agreement with Dr. Irwin. We do, however, feel that in 50 per cent of the cases, the lateral stability was increased and the progress of the curvature was arrested.

I purposely did not go into the technic of the operation. However, we are still leaving the upper end of the fascia anchored in its original bed if we are reinforcing the lower half of the abdomen. If the reinforcement is in the upper half, of course, the fascia has to be completely excised from its bed.

Southern Medical Journal
JOURNAL OF THE
SOUTHERN MEDICAL ASSOCIATION

Copyright, Southern Medical Association, 1941. Published monthly by the Southern Medical Association, Empire Building, Birmingham, Alabama. Annual subscription, $4.00. Single copies, 35c each.

Entered as second-class matter at the Post Office at Birmingham, Alabama, under Act of March 3, 1879. Acceptance for mailing at special rate of postage provided for in Section 1103, Act of October 3, 1917, authorized December 20, 1921.

M. Y. DABNEY, M.D., Editor
C. P. LORANZ, Secretary, Treasurer and General Manager

Volume 34 APRIL 1941 Number 4

EDITORIAL DEPARTMENT

SOUTHERN MEDICAL ASSOCIATION
Thirty-Fifth Annual Meeting
St. Louis, Missouri, November 11-14, 1941

DRUGS FOR PNEUMONIA

For centuries pneumonia has been recognized as one of the important lethal diseases affecting mankind, yet the rather recent advent of type-specific immune serum is regarded by many as the first special advance in the therapy of pneumonia. Also only recently has it been learned that there are thirty-two or more serologically distinct types of pneumococcus, and only a few type-specific effective antisera have been developed. Certainly the victory at best is only a partial one.

Discoveries in medicine often are appreciated slowly and thus applied only gradually. Sulfanilamide is no exception. It was studied to a considerable extent about 1908, but so far as can be ascertained, it was not regarded as a substance useful in treating disease. Following the epoch-making work by Domagk,[1] showing that it was effective in treating animals against certain streptococci, a new vista was opened. Since then, many chemical compounds have been synthesized and tested not only against the streptococcus but also against the pneumococcus and other organisms. Some of these have been effective against the organisms, but many times the margin of safety against an injurious effect on the patient has been too small.

Not until 1938 did Whitby[2] of England offer a real advancement when he demonstrated that sulfapyridine was effective in the treatment of experimental pneumococcal infection. In the same year, Evans and Gaisford[3] showed that this substance was useful in the treatment of lobar pneumonia. It is well to recognize that, although sulfapyridine has a relatively low toxicity, more or less serious toxic manifestations not infrequently follow its administration. In fact, cyanosis, headache, weakness, nausea, febrile reactions, hematuria, calculus formation, anemia, and agranulocytopenia are observed. There is no doubt that sulfapyridine is a beneficial therapeutic agent, and at times even life-saving. Nevertheless, because of its toxicity, it still should be regarded as being in a stage of clinical experimentation.

Most investigators consider sulfapyridine as the forerunner of many compounds yet to be made, tested and their effect evaluated. The mode of action of sulfapyridine is not fully understood, and there is not uniform agreement among investigators in the field. Excellent reports concerning the absorption, excretion and distribution of sulfanilamide, sulfapyridine, sulfathiazole and sulfamethylthiazole have been discussed by Strauss, Lowell, Taylor and Finland.[4]

The most recent report of a new compound effective in the treatment of pneumonia has been made to the Jefferson County Medical Society of Alabama by Dr. T. D. Spies, of Birmingham, and Dr. J. M. Ruegsegger and Dr. Morton Hamburger, Jr., of Cincinnati. They found that the administration of sulfapyrazine to five consecutive cases of pneumococcal pneumonia was followed in each instance by spectacular improvement. It had been shown previously[5] that pyrazine monocarboxylic acid exhibits to some degree the antipellagric action of the corresponding pyridine monocarboxylic acid (nicotinic acid). Recently, Ellingson[6] synthesized a sulfanilamide derivative, analogous to sulfapyridine, in which the pyrazine ring replaces the pyridine ring of the latter. This compound is 2-sulfanilamidopyrazine or sulfapyrazine.

1. Domagk, Gerhard: Deutsche med. Wchnschr., **61**:250, (Feb. 15) 1935.
2. Whitby, L. E. H.: Lancet, **1**:1210, 1938.
3. Evans, G. M.; and Gaisford, W. F.: Lancet, **2**:14, 1938.
4. Strauss, E.; Lowell, F. C.; Taylor, F. H. Laskey; and Finland, M.: Ann. Int. Med., **14**:1360 (Feb.) 1941.
5. Bills, C. E.; McDonald, F. G.; and Spies, T. D.: Sou. Med. Jour., **32**:793 (Aug.) 1939.
6. Ellingson, R. C.: Jour. Amer. Chem. Soc. (in press).

The toxic effects of the sulfanilamide drugs are attributed in part to *in vivo* acetylation which may result in the deposition of the less soluble acetyl derivatives in the urinary tract. *In vitro,* the acetyl derivative of sulfapyrazine is more soluble than the drug itself. The reverse is true of most sulfanilamide drugs. It is, therefore, of interest to report the action of the drug on the first few patients who have received it.

Five cases of nonbacteremic pneumococcal pneumonia in adults under 30 years of age, each with a different type of pneumococcus, were given sulfapyrazine.* Two grams were given at the time the diagnosis was made, and one gram every four hours until the patient had been afebrile for 48 hours. The total average dose in each case was about 25 grams. The patients had had the disease from 1 to 5 days before admission to the hospital. In each case, the temperature became normal within 24 hours after therapy was begun. It is of special interest that no nausea or vomiting occurred; and two of the patients volunteered complete relief from pleural pain. No untoward reaction occurred, and in each instance the action of the drug was dramatic. No other form of therapy was given; and all five patients left the hospital within a week.

In addition to the above cases of pneumonia, this compound was given in doses of over two grams a day to persons with mild pellagra. It showed very slight, if any antipellagric activity, but no toxic effects followed its administration.

*Prepared and supplied by Mead Johnson & Company.

MUSCLE DEGENERATION AFTER NERVE INJURY

Recent studies upon the chemistry of muscle changes after infantile paralysis throw some light upon this disease.

Chemistry is of increasing moment to medicine, though the practitioner at times relies too much upon its work in fields which have hardly been touched.

A physician, after he has said, "It is a chemical change," often feels that he has really explained something. In making a case report, he not infrequently speaks of having ordered a "blood chemistry" and found it "negative," with a confidence equal to that of the drug salesman who knows his product contains vitamins because "they can be seen under the microscope." The "blood chemistry" of the case report, of course, usually means that two to six readily determinable blood constituents, most commonly sugar, nonprotein nitrogen and urea or creatinine, sometimes calcium, phosphorus, or uric acid, have been estimated.

The circulating blood probably contains a trace of every simple chemical element found in sea and earth, of innumerable known compounds and of others the existence of which is just being suspected. The blood probably contains each vitamin, hormone and enzyme, innumerable pigments and inorganic salts, and an unlimited number of decomposition products of protein and carbohydrate metabolism. This is merely to name a few of the current classifications of chemical constituents of the blood, of the existence of which one may be fairly sure. For each of these, there may be a fixed blood level with characteristic variations in health and disease. Hence one may never speak lightly of the patient's blood chemistry, or in this generation claim to have estimated it, but only to have determined the quantity of a few specific constituents.

Little known as is the chemical content of the blood, it is much better known than that of any other tissue. Many statistics are available on its content, because of course it is readily sampled. Chemical changes in muscles during work and after atrophic changes, have recently come in for a considerable share of the attention of chemical analysts, and the correlation of anatomical, chemical and functional studies of muscle is showing progress. Studies of muscles after poliomyelitis and after experimental muscle injury which resembles that of polio are of interest.

Clinically, Herbert Hipps,[1] of Marlin, Texas, has observed the muscles of human beings after poliomyelitis and shown that they may exhibit limited areas of fatty degeneration and fibrosis which interfere with function. Under certain conditions the muscles may be capable of operative improvement. The fatty areas which act as insulation, preventing normal contraction throughout the muscle length, may sometimes be eliminated and normal muscle made continuous. Thus the muscle may occasionally be made to function again.

Study of the various steps in progression of the fatty and fibrous degeneration may provide

1. Hipps, Herbert E.: Muscle Pathology in Anterior Poliomyelitis: Its Relation to Function. Sou. Med. Jour., 34:135 (Feb.) 1941.

help in their correction. Levine, Hechter and Soskin,[1] in the Michael Reese Hospital in Chicago, have recently reviewed studies on the chemistry of muscle atrophy in conditions which resemble those after poliomyelitis, and they have made some further contributions to its understanding.

Muscular atrophy, they say, follows injury to the anterior horn cells in infantile paralysis, and it may be duplicated experimentally in the rat by section of motor nerve connections. Histologically the resulting atrophy is shown as loss of muscle protein with replacement by fibrous tissue and fat. This might occur because protein is rapidly destroyed in the muscle, or because it is not resynthesized after nerve injury.

Severance of the motor nerves leads to a disorganized but increasing activity of muscle fibers with fibrillation beginning in about four days.[2] This is followed by exhaustion of the carbohydrate stores, which within two weeks are at a low level. Muscle glycogen and creatine phosphate are at a low level and ability to restore them after muscular effort is greatly impaired. The eventual atrophy the Chicago workers believe in the rat to be a result of overwork, and to be capable perhaps of some control by drugs. Atropine, they believe, decreased the rate of atrophy of the denervated gastrocnemius muscle of the rat, while prostigmine increased it.

Nerve injury thus is followed by failure of adequate nutrition of the muscle and depletion of necessary glycogen and phosphate compounds.

Nerves under natural conditions may be injured by physical violence, by bacterial attack, or presumably by malnutrition as from deficiency of vitamin B_1. Whether muscle fibrillation in itself may be taken as evidence of motor nerve injury is a question for study.

HYSTERECTOMY AND THE OVARIES

Hysterectomy is not a rare operation in young women, and it is the general impression that aside from sterilization, removal of the uterus produces little general physiologic effect. Fluhmann noted that the ovaries of a young woman examined a year after total hysterectomy showed no recent corpus luteum, but a large number of atretic cystic follicles.[2] Mishell and Motyloff,[2] of New York City, investigated the effect of hysterectomy upon the ovaries of rabbits, noted certain changes and have made attempts at replacement therapy, which suggest the possibility of existence of an endometrial hormone. Rabbits, they note, examined three months after hysterectomy, show atrophy of the follicular apparatus of the ovaries, with precocious regression of these glands. There were abnormalities in the growth of the follicles, atypical development and degeneration of corpora lutea, and compensatory hypertrophy of the interstitial tissue which terminated in cellular degeneration. The process of follicular proliferation could be regulated to some extent by treatment with an oily extract of cow's endometrium. The extract did not prevent the formation of corpora lutea, though it increased the longevity of the corpus luteum. It protected the functional elements of the ovary and retarded the process of atrophy. In the controls, the nonoperated animals, there was no evidence of atrophy, and there were no corpora lutea. In normal nonoperated animals which were treated with endometrial extract, there were no unusual changes.

More effective in prolonging the life of the ovary of hysterectomized animals was implantation of pieces of endometrium between the peritoneum and muscular coats of the abdominal wall. If these transplants showed definite secretory activity after three months, marked functional activity of the ovary was seen.

If hysterectomy is followed by premature ovarian degeneration, one would expect that it should also be accompanied by changes in the portion of the anterior pituitary gland which is stimulated by the ovaries. A chain of alterations would thus be initiated by removal of the uterus.

1. Levine, R.; Hechter, O; and Soskin, Samuel: Biochemical Characteristics of Denervated Skeletal Muscle at Rest and After Direct Stimulation. Amer. Jour. Physiol., **132**:336 (March) 1941.
2. Mishell, D. R.; and Motyloff, Leon: The Effect of Hysterectomy Upon the Ovary. Endocrinology, **28**:436 (March) 1941.

TWENTY-FIVE YEARS AGO

From Journals of 1916

British Diet.[1]—The quantity of food required to maintain in health a person not engaged in strenuous muscular exercise is much less than is generally supposed. * * * The following is the diet of a London postman, aged 26, who walks about fifteen miles in the day and on some beats has to mount some five thousand steps daily * * * 5:00 a. m., a piece of toast and a cup of tea; 9:00 a. m., one rasher of bacon, four moderate slices of bread and butter, two cups of tea; 2:00 p. m., a chop or cut off the joint, four potatoes and green vege-

1. Campbell, Harry: The Limitation of the Quantity of Food to a Sufficiency. Food Economics in Relation to the War. Lancet, **190**:792 (April) 1916.

tables; 6:00 p. m., a bloater (or some other fish), four slices of bread and butter, and one cup of tea.

Jaundice at Gallipoli.[2]—Drs. Sarrailhe and Clunet have reported before the Societe Medicale des Hospitaux de Paris numerous cases of icterus which they observed at Gallipoli. The camp jaundice always appeared under the same conditions, that is, in fatigued troops confined for several weeks in cramped quarters and demoralized by a poor diet and a trying climate * * * the jaundice was due to hepatic localization of a paratyphoid virus.

Warsaw Meeting.[3]—The German Congress for Internal Medicine will be held in Warsaw May 1 and 2. Last year a similar Congress for Surgery was held in Brussels * * * the diseases which are of particular importance at this time, especially typhoid, typhus, cholera, diarrhea, diseases of the heart and nephritis will be discussed. Attendance will be limited to the military and civil physicians of the German Empire and its allies. Physicians of neutral countries and countries with which the central powers are at war will not be admitted.

2. Paris Letter. J.A.M.A., **66**:1126 (April) 1916.
3. Berlin Letter. Ibid., p. 1039.

Book Reviews

Clinical Pellagra. By Seale Harris, M.D., Professor Emeritus of Medicine, University of Alabama, Birmingham, Alabama, assisted by Seale Harris, Jr., M.D., Formerly Assistant Professor of Medicine, Vanderbilt University, Birmingham, Alabama. 494 pages, illustrated. St. Louis: The C. V. Mosby Company, 1941. Cloth $7.00.

In his foreword to this book E. V. McCollum says: "Nowhere else is there so complete a history of investigations relating to pellagra, and the assembled quotations and comments make a fascinating story." After studying Dr. Harris' book the reviewer subscribes wholeheartedly to this opinion. The primary points of value in the volume are two: first, there is an excellent discussion of the various clinical aspects of this important disease, and second, and most important, there is a lucid presentation of the author's point of view about it; and this point of view is probably the most scientific attitude toward the subject which has ever been written. It may be summarized by the following lines from the preface:

"There seems to be sufficient evidence to conclude that the essential factor in the production of pellagra is a deficiency of nicotinic acid, the pellagra-preventive factor in vitamin B, and enzyme activator; but the underlying pathogenesis of the nicotinic acid deficiency in a large proportion of cases probably is an insufficiency of the stomach and liver."

In the enthusiasm which has followed the brilliant demonstration of the role of nicotinic acid in pellagra, there has been a tendency to lose sight of the importance of the other factors concerned in this disease. Such a tendency can best be corrected by a careful perusal of this book. The author quotes in detail the experiments of Sydenstricker and Thomas, which indicate very strongly that in addition to the extrinsic factor (nicotinic acid) there is an intrinsic factor which has many similarities to the intrinsic factor described by Castle in pernicious anemia. Both seem to be formed in the stomach and stored in the liver. Such an observation, which was apparently first carried out by Spies and later elaborated by Sydenstricker and Thomas, would seem now to have been demonstrated beyond reasonable question. Such a concept will serve to account for the frequency of pellagra in persons with alcoholism and diseases of the intestinal tract and the liver. It also accounts for the failure of many patients with typical pellagra to respond to nicotinic acid alone as well as for numerous other therapeutic aspects of the disorder.

Although "Clinical Pellagra" is written primarily from a personal point of view and relates many of the experiences of the author, there are several chapters written by other authors. These constitute a valuable addition to the book, which can be read with profit by every clinician who comes in contact with the disease and by every investigator who is studying the general problems of nutritional deficiency.

Strange Malady: The Story of Allergy. By Warren T. Vaughan, M.D. 268 pages, illustrated. New York: Doubleday, Doran & Co. Cloth $3.00.

This book can be recommended to any one, either lay or professional, who is interested in the story of the development of modern medicine. The development of allergy or any other branch of the field is naturally bound up in the development of the whole. Nowhere is this fact better demonstrated than in this book. The present author is peculiarly fitted to write this story, having acquired much of it from his father, the famous Dr. Victor C. Vaughan.

The inclusion of photographs of many physicians who are famous for the roles they have played in the development of allergy and of modern medicine gives added interest. The various chapters are illustrated with cartoons and charts which help to make clear their meanings.

"Strange Malady" is sponsored by the American Association for the Advancement of Science, which fact alone will be recommendation enough for many readers. The book is well written and easy reading and is worth the time of anyone at all interested in the subject.

The Diagnosis and Treatment of Diseases of the Heart. By Henry Christian, M.D., Sc.D. (Hon.), LL.D., F.A.C.P. (Hon.), F.R.C.P. (Can.), Hersey Professor of the Theory and Practice of Physic, Emeritus, Harvard University. 569 pages. New York: Oxford University Press, 1940. Cloth $7.00.

The author of this book has been for many years one of the leading students of heart disease in this country. At a time when most cardiologists were misled in their treatment of heart failure by inaccurate interpretation of some of the experiments on animals and had concluded that digitalis is of little or no value in any type of heart failure except that associated with auricular fibrillation, Dr. Christian insisted, on the basis of carefully controlled studies, that the drug was of great

value in many patients with regular rhythm. He writes with a wide experience and with a great deal of authority.

The approach to the subject is primarily from the anatomic and etiologic point of view, and the various subjects discussed involve the diagnosis and treatment of the several different types of disease which effect the endocardium, pericardium and myocardium. From the standpoint of the etiologic and pathologic viewpoints in heart disease the book is somewhat better than from the more recently developed functional viewpoint. It can, however, be read with profit by anyone, because it embodies the personal experiences of a leading student in this important field.

Electrocardiographic Patterns: Their Diagnostic and Clinical Significance. By Arlie R. Barnes, M.D., Mayo Clinic, Rochester, Minnesota. 195 pages, illustrated. Springfield, Illinois: Charles C. Thomas, 1939. Cloth $5.00.

When the electrocardiogram was first introduced into clinical medicine it was used primarily as a method of detecting and analyzing cardiac irregularities. The usefulness of the method in this respect is somewhat less than twenty years ago, because clinicians now are so much more familiar than they were with arrhythmias that the special instrumental methods are rarely needed to make the proper diagnosis. However, the electrocardiogram has developed another and entirely different field of usefulness, namely, in the detection of various types of myocardial disease, and particularly such types as follow disturbances in the coronary circulation. For the developments in this field the work of F. N. Wilson and his pupils is primarily responsible. However, other individuals have also made notable contributions to the subject and very few of them have made more important contributions than has Dr. Barnes, whose work a number of years ago on relation to the T-wave change in different types of coronary disease was of fundamental significance. In this book Dr. Barnes summarizes his observations, which have extended now over a period of a good many years, and which have enabled him to predict the location of myocardial lesions with a high degree of accuracy. There is also an excellent discussion of electrocardiographic patterns in relation to pericarditis.

Heart Failure. By Arthur M. Fishberg, M.D., Associate in Medicine, Mount Sinai Hospital, New York City. Second Edition. 829 pages, illustrated. Philadelphia: Lea & Febiger, 1940. Cloth $8.50.

The author of this book possesses to a very unusual degree the capacity to combine the purely clinical aspects of the subject with an interpretation of the recent advances in the study of the physiology of the circulation. He has surveyed all of the pertinent literature with great care and has been able to pick out those studies which are important and to integrate these into the clinical picture of the several circulatory syndromes. Since the publication of the previous edition considerable new work has appeared and this is included in the new edition, which has been entirely rewritten. The practical part of the work, which deals with diagnosis and treatment, is excellent and the chapters which are concerned with the theoretical aspects of the mechanism of the various clinical manifestations of circulatory failure are unsurpassed.

The first several chapters in the book concern a general discussion of some of the important circulatory functions, such as cardiac output, velocity of blood flow, blood volume, and arterial and venous pressure. In the next several chapters the author deals with the pathologic physiology and mechanism of the important manifestations of heart disease, such as dyspnea and edema. This is followed by a discussion of the disturbances in circulation in the lungs, liver, kidneys and nervous system. Special signs of cardiac disease are then discussed, including excellent considerations of cardiac enlargement, gallop rhythm, murmurs, and pain. There are then several chapters dealing with the different forms of heart failure and an excellent discussion of the failure of the peripheral circulation. The final section of the book deals with the treatment of the various circulatory syndromes.

Because of its unique qualities this book can be profitably studied by everyone who is interested either in the physiology of the circulation or in the practical care of patients with heart disease. Even the most expert cardiologist can learn much from a careful perusal of Dr. Fishberg's book.

Hypertension and Nephritis. By Arthur M. Fishberg, Associate in Medicine, Mount Sinai Hospital, New York City. Fourth Edition. 761 pages, illustrated. Philadelphia: Lea & Febiger, 1939.

This is the fourth edition of a book which is now generally recognized as a classic in medical literature. During the period which has elapsed since the appearance of the third edition, a very large volume of new knowledge has been added to the subject. So great is this in quantity and so important is it that the new edition, which gives full emphasis to the more recent advances in the subject, is practically a new book. The subject is approached in its broadest aspects and is considered fully from the standpoint of the abnormalities in physiology, chemistry and pathology. However, the clinical sections are by no means neglected and the book is full of practical information as regards diagnosis and treatment. Beginning with a discussion of renal function, the various clinical manifestations of renal disease such as albuminuria, edema and uremia are discussed in elaborate and painstaking detail. The various types of nephritis are considered in a number of concise but exhaustive chapters. The final part of the book deals with the subject of hypertension, which is considered from all points of view.

The newer developments in these various fields have been carefully sifted by the author and he has included in the new edition references to most of the important new work as well as excellent critical summaries of its significance. This has been very difficult because the field is changing rapidly, but the task has been performed in excellent fashion. There is certainly no book in the English language on this subject which compares favorably with this volume, and probably there is no book in any language which presents the same well-rounded critique and the same combination of sound clinical conservatism with a complete willingness to accept new ideas when they are backed by adequate evidence.

The Doctor and His Patients: The American Domestic Scene as Viewed by the Family Doctor. By Arthur E. Hertzler, M.D., Author of "The Horse and Buggy Doctor." 316 pages. New York: Harper & Brothers, 1940. Cloth $2.75.

The author of "The Horse and Buggy Doctor," a recent best seller, takes up in intimate detail the domestic scene in his latest book, "The Doctor and His Patients." The chapter headings with a miltonesque flavor: "The Prelude to Paradise," "Paradise Illustrated," "Dream of Paradise," and so on to "Purgatory," and finally "Paradise Earned," begin with the child in the home. The theme is carried with much homely philosophy and reminiscence through adolescence, marriage and the honeymoon, on to old age. The basis of the whole book is sex and even though a wide field is covered, it is never far from this basis.

For the layman the book may reveal many phases of domestic life but poorly understood generally. For the physician the anecdotes and cases bring to mind similar instances in his own practice. Both the layman and the physician may profit greatly by the very wise and serious observations inserted liberally throughout the volume.

The Doctor and the Difficult Child. By William Moodie, M.D., F.R.C.P., D.P.M., Medical Director, London Child Guidance Clinic and Training Center. 214 pages. New York: The Commonwealth Fund, 1940. Cloth $1.50.

An English psychiatrist of wide experience discusses the emotional disturbances of childhood. He stresses the importance of a full history, including the environment, in the home and school, the interpretation of play, fantasies, and so on. Many helpful suggestions are made toward winning the confidence of children. The various behavior problems, such as stealing, lying, enuresis and nervousness, are discussed and suggestions made regarding their management.

The book is a valuable aid in child guidance.

Methods of Treatment. By Logan Clendening, M.D., Clinical Professor of Medicine, Medical Department of the University of Kansas, and Edward H. Hashinger, A.B., M.D., Clinical Professor of Medicine, Medical Department of the University of Kansas, Kansas City, Mo. 977 pages, illustrated. St. Louis: The C. V. Mosby Company, 1941. Cloth $10.00.

Here is really a most valuable book. Where other works name the treatment to be given this one tells how to give it. The avowed purpose is to furnish an outline of all the methods of treatment in internal medicine. It gathers together material widely scattered in medical literature; as, for instance, descriptions of the technic of spinal puncture, blood transfusion, the wet pack and the ketogenic diet. And not only is the technic of a method of treatment painstakingly given, but usually a discussion of the rationale behind it. Texts on therapeutics and pharmacology are usually devoted exclusively to drugs. Here all therapeutic procedures are brought together within the compass of one volume.

The first part describes each procedure under the heading of drugs, diet, hydrotherapy, and so on. The second considers the application and results to be expected under the heading of the various diseases. In the present revision the work has been made to conform to the eleventh edition of the United States Pharmacopoeia.

Both Dr. Clendening and Dr. Hashinger are outstanding men in the field of clinical medicine. The former is also a popular writer of note and his crisp comments in the second part enliven the book.

The 138 illustrations are of much practical value in clarifying technic.

Acute Infectious Diseases: A Handbook for Practitioners and Students. By J. D. Rolleston, M.A., M.D. (Oxon.), F.R.C.P. (Lond.), F.S.A., Formerly Medical Superintendent, Western Hospital, London; Editor British Journal of Children's Diseases, and G. W. Ronaldson, M. D. (Glasg.), D.P.H. (Oxon.), Medical Superintendent, Southeastern Hospital, London. Third Edition. 477 pages. St. Louis: The C. V. Mosby Company, 1940. Cloth $4.50.

The subjects are exhaustively treated and the bibliography is quite complete. The reviewer notes with pleasure the references made to American authorities and the agreement with their prevailing ideas as to etiology and treatment, which represent quite a departure from previous English texts on pediatric subjects. The absence of illustrations will be no disappointment to many readers, although modern chromatic photography has overcome most of the former objections to lack of fidelity in color illustrations. This is an excellent book.

The Fundamentals of Nutrition. By Estelle E. Hawley, Ph.D., and Esther E. Maurer-Mast, M.D., University of Rochester, School of Medicine and Dentistry, Rochester, New York. 477 pages, illustrated. Springfield, Illinois: Charles C. Thomas, 1940. Cloth $5.00.

This book represents a rather unusual achievement in that it has been written by a large number of different individuals, all of whom are or have been associated with the School of Medicine of the University of Rochester. It combines most of the advantages of a simple manual of dietetics with a scientific discussion of the fundamental and practical aspects of nutrition. Although the utilization of a group of individuals is subject to the usual disadvantage of causing some lack of coherence and results in some overlapping, this disadvantage is overcome by the advantage of having each chapter written by an individual with a wide experience in the field to be discussed.

The first half of the book is divided into a section on metabolism, a section on nutrition, and a part concerned with dietotherapy. The first two of these sections do not offer any new knowledge, but do represent concise summaries of existing knowledge. The section on the dietary management of various diseases is well written and can be considered authoritative.

The second half of the book supplies a great deal of practical information in terms of calculation of diets, dietary tables, tables of food composition, and so on. There are also a number of recipes and some methods of assay for various vitamins as well as specific diets for various types of diseases. The volume is a useful reference book and a valuable book to have, although it is difficult to read because of the wide variety of subjects covered.

Manual of Clinical Chemistry. By Miriam Reiner, M.Sc., Assistant Chemist to the Mount Sinai Hospital, New York. 296 pages, illustrated. New York: Interscience Publishers, Inc. Cloth $3.00.

Here is a timely methods book which should be received with a ready welcome. Although it is arranged in a cook book manner, the outline form is attractive. The author makes no attempt at elaborate discussion of methods, but gives essential information for actual performance of various routine clinical examinations of blood, urine, cerebrospinal fluid, feces, and gastric juice. Methods for sulfanilamide, arsenic, lead, mercury and barbiturates are given. A valuable section on functional tests includes tests for renal function, hepatic function, blood volume, prothrombin and creatinine tolerance. Procedures for the determination of vitamins A, B and C are given. There are methods for certain sex hormones, renal and biliary calculi and milk analysis.

A great many difficult procedures are simplified by outlining and illustrating when necessary. This book has a definite place in the clinical laboratory, but it must be supplemented with standard texts on biochemistry.

Southern Medical News

AMERICAN ACADEMY OF PEDIATRICS, REGION 2

The American Academy of Pediatrics, Region 2, will hold its annual meeting at the John Marshall Hotel, Richmond, Virginia, Thursday and Friday, April 24 and 25, 1941. In the scientific program the following subjects will be considered: "Mental Health of the Child as Related to National Defense;" "Nutrition of the Child as Related to National Defense;" "Communicable Diseases and Their Relations to the Child During National Defense;" and "Food Contaminations and Poisons." All physicians who are members of their state medical societies are invited to attend the program sessions. The states comprising Region 2 are: Alabama, Arkansas, District of Columbia, Florida, Georgia, Kentucky, Louisiana, Mississippi, North Carolina, Oklahoma, South Carolina, Tennessee, Texas, Virginia and West Virginia. Dr. Hugh Leslie Moore, Dallas, Texas, is Regional Chairman, and Dr. J. B. Stone, Richmond, Virginia, is General Chairman of the local committee.

ALABAMA

The Alabama Association of Medical Technicians will hold their annual convention at the Redmont Hotel, Birmingham, Friday and Saturday, May 2 and 3. The officers are: Miss Evelyn Martin, President, Birmingham; Mrs. Fannie Mae Frank, Secretary, Montgomery; Mrs. Cannie Mayfield, Treasurer, Tuscaloosa; and Miss Nell Stockton, Chairman of Program Committee, Birmingham.

The Jefferson Hospital, Birmingham, a sixteen-story structure with a capacity for 650 patients, has been erected at a cost of $2,250,000, and was dedicated December 29. Dr. W. Lawson Shackelford, formerly Superintendent of the Good Samaritan Hospital, West Palm Beach, Florida, has been appointed Director. Members of the Operating Board are: Dr. Harry Lee Jackson, Dr. Earle Drennen and Dr. James R. Garber.

Dr. W. Lawson Shackelford, Birmingham, has been awarded a Certificate of Honor by the American Hospital Association in recognition of excellent service rendered the Association and the National Hospital Day Committee during the past fifteen years.

A new Infantile Paralysis Center at Tuskegee Institute, adjoining the John A. Andrew Memorial Hospital, Tuskegee, which was financed by a grant of $161,350 from the National Foundation for Infantile Paralysis, was dedicated on January 15.

Dr. Karl B. Benkwith announces the opening of his office in the Bartlett Building, Montgomery, with practice limited to ophthalmology and ophthalmic surgery.

Dr. Francis M. Thigpen announces the opening of his office at 401 South Court Street, Montgomery, for the practice of general surgery and proctology.

DEATHS

Dr. John W. Boggess, Jr., Guntersville, aged 38, died March 8.

Dr. J. L. Weldon, Lanett, aged 57, died February 28.

ARKANSAS

Carroll County Medical Society has elected Dr. D. K. McCurry, Green Forest, President; Dr. W. A. Butt, Green Forest, Vice-President; and Dr. A. L. Carter, Berryville, Secretary-Treasurer.

Clay County Medical Society has elected Dr. W. J. Blackwood, Rector, President; Dr. W. E. Turner, Jr., Piggott, Vice-President; and Dr. J. E. McGuire, Piggott, Secretary-Treasurer.

Drew County Medical Society has elected Dr. J. S. Wilson, President; Dr. R. D. Dickens, Vice-President; and Dr. J. P. Price, Secretary-Treasurer, all of Monticello.

Montgomery County Medical Society has elected Dr. J. B. Stueart, Norman, President; Dr. G. E. Watkins, Mount Ida, Vice-President; and Dr. J. H. McLean, Caddo Gap, Secretary-Treasurer.

The Arkansas Medical Society and the Arkansas Dental Association have approved a plan outlined by the National Youth Administration, inaugurating a youth health program in Arkansas as a part of the defense movement. Dr. Sidney J. Wolfermann, Fort Smith, has been appointed for the State Medical Society on an Advisory Committee to cooperate in the movement, and Dr. William B. Grayson, Little Rock, for the State Board of Health.

Dr. James W. Branch, Hope, has been ordered to active duty with the Army Medical Corps and assigned to Station Hospital, Fort Knox, Kentucky.

Dr. W. A. Snodgrass, Jr., Pine Bluff, has entered active military service and is stationed at the Station Hospital, Camp Robinson.

Dr. Vann C. Binns, formerly of Pine Bluff, is now on duty with the First Medical Squadron, Fort Bliss, Texas, as Captain, Medical Corps.

Dr. A. B. Tate, formerly of Augusta, has been assigned Medical Director at Clarksville.

Dr. A. F. Hayes, formerly of Russellville, has been assigned Health Director at Augusta.

Dr. B. E. Hendrix, Gilham, has been elected President of the Bank of Horatio for the thirty-fifth consecutive time.

Dr. J. B. Jameson and Dr. R. B. Robins have been elected Directors of the Camden Chamber of Commerce.

Dr. C. H. Lutterloh, Hot Springs National Park, and Dr. F. H. Jones, Piggott, have been elected President-Elect and Arkansas Vice-President, respectively, of the Mid-South Postgraduate Medical Assembly.

Dr. Wm. H. Newkirk, Captain, Medical Corps, U. S. Army, Camp Robinson, has been elected Vice-President of the Little Rock Military Club.

Dr. B. P. Briggs, Little Rock, has been elected a Fellow of the American Academy of Pediatrics.

Dr. L. J. Harrell has moved into new offices at Prescott.

Dr. Joe F. Rushton has been elected a Director of the Citizen's Bank at Magnolia.

Dr. W. J. B. Williams, Des Arc, and Miss Lorene Kloss, Beebe, were married January 1.

DEATHS

Dr. Henry Herbert Darnall, Fulton, aged 61, died February 11.

DISTRICT OF COLUMBIA

The new Tuberculosis Annex and Nurses' Home of Freedmen's Hospital, Washington, built at a cost of $700,000, were dedicated January 21. Dr. T. Edward Jones, Director-in-Chief of the Hospital, presided. The PWA financed the construction of the buildings.

Continued on page 38

Treatment of disease, to a great extent, is built on confidence. The patient believes in the competence of his physician, and the doctor, in turn, relies upon the company whose products he prescribes.

EXTRALIN
(Liver-Stomach Concentrate, Lilly)

'Extralin' provides the antipernicious-anemia principle in a highly concentrated form for oral use. With 'Extralin' the blood count may be maintained at normal levels with the least amount of inconvenience to the patient. Nine to twelve pulvules daily constitute an average maintenance dose.

ELI LILLY AND COMPANY
Principal Offices and Laboratories, Indianapolis, Indiana, U. S. A.

Harvard Medical School

COURSES FOR GRADUATES

Surgical Technique

June 16-27—Peter Bent Brigham Hospital and Harvard Medical School. Fee, $200.

Urology

June 16-28—Massachusetts General Hospital
Fee, $80

Internal Medicine—Diagnosis and Treatment

June 18-July 30—Massachusetts General Hospital
Fee, $200

Modern Diagnosis and Treatment of Heart Disease

July 1-31—Peter Bent Brigham Hospital. Fee, $150.

Pediatrics

July 1-31—Massachusetts General Hospital. Fee, $125.

Cardiology—Advanced Cardiology

August 1-30—Cardiology.
September 2-30—Advanced Cardiology
Massachusetts General Hospital.
Fee, $150, for each course.

For further information, apply to

Assistant Dean, Courses for Graduates
Harvard Medical School, Boston, Massachusetts

The Tulane University of Louisiana

SCHOOL OF MEDICINE

Review Courses in all branches of medicine annually—January through March.

COURSES leading to specialization in otolaryngology and in ophthalmology.

Special, short time, intensive courses in certain fields may be arranged.

For detailed information write

Director
Department of Graduate Medicine
1430 Tulane Avenue, New Orleans, La.

Continued from page 452

Children's Hospital, Washington, is the recipient of a new dental unit presented by the Washington Variety Club.

The Red Cross Recreation Building of St. Elizabeth's Hospital, Washington, was destroyed by fire of undetermined origin February 4, the estimated loss being $25,000.

Dr. Thomas Parran, Surgeon General of the United States Public Health Service, Washington, sailed for England in January as one of the officials included in the American Commission to study health conditions, epidemic control, transportation and evacuation of children in Great Britain. The Commission is sponsored jointly by the Division of State and Local Cooperation of the National Defense Advisory Commission and the War Department.

Dr. William Gerry Morgan, Washington, has been named Chairman of the Washington Branch of the American Bureau of Medical Aid to China.

FLORIDA

Brevard County Medical Society has elected Dr. T. C. Kenaston, Cocoa, President; Dr. G. H. Christie, Titusville, Vice-President; and Dr. I. K. Hicks, Melbourne, Secretary-Treasurer, re-elected.

Putnam County Medical Society has elected Dr. C. M. Knight, Palatka, President, and Dr. J. Worth Brantley, Grandin, Secretary-Treasurer.

Sarasota County Medical Society has elected Dr. J. C. Patterson, President; Dr. T. W. Taylor, Vice-President; and Dr. Stanley T. Martin, Secretary-Treasurer, all of Sarasota.

Washington County Medical Society has elected Dr. N. J. Dawkins, President, and Dr. B. W. Dalton, Secretary-Treasurer, both of Vernon.

The Committee on Postgraduate Instruction of the State Medical Association announces that its Short Course will be held at the George Washington Hotel, Jacksonville, June 23-28, inclusive.

The Dillman Pavillion, a new wing of the Good Samaritan Hospital, West Palm Beach, with a capacity of fourteen rooms, was opened for use January 5.

Dr. William H. Pickett, Jacksonville, has been appointed State Health Officer to fill the unexpired term of Dr. A. B. McCreary, who died recently. Dr. J. N. Paterson, Director of Laboratories of the State Board of Health since 1938, has been named Assistant Health Officer. He will continue to direct the activities of the Laboratory.

Dr. John O. Barfield, Miami and Apalachicola, is Director of the City-County Health Department at Panama City.

Dr. A. L. Stebbins, Director of the City-County Health Unit at Pensacola, has completed postgraduate work in obstetrics at the Lying-In Hospital of the University of Chicago.

Dr. Henry Fuller, formerly of Mulberry, is now associated with Dr. Herman Watson, Dr. S. Edgar Watson and Dr. Jere W. Annis at Lakeland, his practice limited to diagnosis and internal medicine.

Dr. Guy R. Stoddard is now associated with Dr. Harrison A. Walker in the Lincoln Road Building, Miami Beach, in the practice of surgery.

Dr. Leander J. Graves, Tallahassee, Director of the Leon County Health Unit, was chosen President of the Florida Public Health Association at its meeting in December. Dr. Edward M. L'Engle, Jacksonville, is Secretary-Treasurer. Orlando will be the 1941 meeting place.

Dr. Mary Stewart Howarth and Mr. C. R. M. Sheppard, both of DeLand, were married January 25.

DEATHS

Dr. Albert H. Freeman, Ocala, aged 75, died January 11.
Dr. A. B. McCreary, Jacksonville, aged 45, died January 24.

GEORGIA

Baldwin County Medical Society has elected Dr. Chas. B. Fulghum, Milledgeville, President; Dr. W. A. Bostick, Hardwick, Vice-President; and Dr. C. L. Howard, Milledgeville, Secretary-Treasurer.

Butts County Medical Society has elected Dr. B. F. Akin, President, and Dr. R. L. Hammond, Secretary-Treasurer, both of Jackson.

Clarke County Medical Society has elected Dr. Lewis S. Patton, President; Dr. Marion A. Hubert, Vice-President; and Dr. Loree Florence, Secretary-Treasurer, all of Athens.

Haralson County Medical Society has elected Dr. E. F. Sanford,

Continued on page 40

when appetite lags....

employ this elixir of natural B-complex and glycerophosphates

For the anorexia and sluggish digestion so frequently encountered during the winter months, Elixir 'B-G-Phos' offers a stimulating and exceptionally pleasant tonic combining the advantages of the entire B-complex from *natural sources* with glycerophosphates.

Elixir 'B-G-Phos' includes Vitamins B_1, B_2, and B_6 together with the filtrate factor, nicotinic acid, and other natural factors of the entire B-complex, combined with the glycerophosphates of calcium, sodium, potassium, and manganese.

Elixir 'B-G-Phos' not only tends to correct B-complex deficiencies but stimulates the appetite and helps to re-establish intestinal motility. Thus, disturbances of elimination are corrected and digestive functions are improved.

Elixir 'B-G-Phos' is supplied in pint and gallon bottles.

One Tablespoonful
Three Times a Day before Meals

Elixir 'B-G-Phos'

Sharp & Dohme

Human Convalescent and Immune Serums

For passive immunization against measles, scarlet fever, and whooping cough, and for treatment of scarlet fever and whooping cough.

THESE SERUMS ARE SOLD AT COST PLUS MAILING CHARGES

24-hour service—telegraph orders will receive prompt attention.

National Institute of Health License No. 139

The Philadelphia Serum Exchange
Children's Hospital of Philadelphia
1740 Bainbridge Street, Philadelphia, Pa.

Continued fro mpage 38

Buchanan, President; Dr. C. W. Downey, Tallapoosa, Vice-President; and Dr. C. H. Allen, Bremen, Secretary-Treasurer.

Henry County Medical Society has elected Dr. H. C. Ellis, McDonough, President; Dr. R. L. Crawford, Locust Grove, Vice-President; and Dr. E. G. Colvin, Locust Grove, Secretary-Treasurer.

Jenkins County Medical Society has elected Dr. Q. A. Mulkey, President; Dr. I. S. Giddens, Vice-President; and Dr. J. F. Folk, Secretary-Treasurer, all of Millen.

Mitchell County Medical Society has elected Dr. C. A. Stevenson, Camilla, President; Dr. M. M. Burns, Pelham, Vice-President; and Dr. C. L. Roles, Camilla, Secretary-Treasurer.

Morgan County Medical Society has elected Dr. J. L. Porter, Rutledge, President; Dr. D. M. Carter, Madison, Vice-President; and Dr. W. C. McGeary, Madison, Secretary-Treasurer.

Monroe County Medical Society has elected Dr. W. J. Smith, Juliette, President; and Dr. G. H. Alexander, Forsyth, Secretary-Treasurer.

Richmond County Medical Society has elected Dr. S. J. Lewis, Augusta, President, and Dr. E. R. May, Lincolnton, Secretary-Treasurer.

Spalding County Medical Society has elected Dr. M. M. Head, Zebulon, President; Dr. W. C. Miles, Griffin, Vice-President; and Dr. J. T. Leslie, Griffin, Secretary-Treasurer.

Thomas County Medical Society has elected Dr. Chas. H. Watt, Thomasville, President; Dr. J. N. Isler, Meigs, Vice-President; and Dr. Herbert F. Readling, Thomasville, Secretary-Treasurer.

Telfair County Medical Society has elected Dr. Jno. T. Persall, Jr., McRae, President; Dr. S. T. Parkerson, McRae, Vice-President; and Dr. Foster P. Harbin, Lumber City, Secretary-Treasurer.

Tri-County Medical Society has elected Dr. C. K. Sharp, Arlington, President; Dr. S. P. Holland, Blakely, Vice-President; and Dr. W. C. Baxley, Blakely, Secretary-Treasurer.

Wilkes County Medical Society has elected Dr. A. W. Simpson, Jr., President; Dr. L. R. Casteel, Vice-President; and Dr. R. G. Stephens, Secretary-Treasurer, all of Washington.

Dr. Fred F. Rudder, Atlanta, received the Dr. L. C. Fischer Award for the best original work this year. Dr. Thomas S.

Continued on page 42

THE NEW YORK POLYCLINIC
MEDICAL SCHOOL AND HOSPITAL

(ORGANIZED 1881)
THE PIONEER POST-GRADUATE MEDICAL INSTITUTION IN AMERICA

Radiology

A comprehensive review of the physics and higher mathematics involved, film interpretation, all standard general roentgen diagnostic procedures, methods of application and doses of radiation therapy, both x-ray and radium, standard and special fluoroscopic procedures. A review of dermatological lesions and tumors susceptible to roentgen therapy is given, together with methods and dosage calculation of treatments. Special attention is given to the newer diagnostic methods associated with the employment of contrast media such as bronchography with Lipiodol, uterosalpingography, visualization of cardiac chambers, perirenal insufflation and myelography. Discussions covering roentgen departmental management are also included.

Plastic Reparative Surgery

The course comprises examination of patients; tests, models and photographs; diagnosis and selection of method of correction; the properties of various orders of skin grafts and variance in their application; bone, cartilage and nerve grafts; readjustments and replacements; fresh wound treatment; pre-operative care; anesthesia; operative procedures; wound closing and minimum scar; follow-up and infection problems; keloids. The course covers the field of correction of disfigurements and replacement of traumatic loss and congenital deficiency. Exposition of cases, lectures and cadaver demonstrations.

FOR INFORMATION ADDRESS
MEDICAL EXECUTIVE OFFICER
345 West 50th Street NEW YORK CITY

DIABETIC DIETS *can be improved and varied with* KNOX GELATINE *(U.S.P.)*

We have compiled a booklet which may save you time and trouble in preparing diets for your diabetic patients. It is called "Feeding Diabetic Patients—Young and Old."

The booklet contains a discussion of the principles of diabetic feeding, practical tables of food composition expressed in percentages of 100-gram portions, sample menus, and 33 pages of simple, economical and attractive recipes with composition and caloric value of all foods and recipes.

The use of Knox Plain (Sparkling) Gelatine is explained, with examples of how Knox Gelatine can give variety to appetizing "full-sized" meals without interfering appreciably with caloric requirements. (Knox is 85% to 87% protein—entirely free of sugar.) It contains a majority of the food amino acids and has been shown to supplement protein of nearly every variety of food.

Also included in this booklet are typical dietary prescriptions representing Normal Carbohydrate Maintenance, Restricted Carbohydrate High Fat, Diabetic Reducing and Children's Diabetic diets.

The coupon below will bring you as many of these diet booklets as you require, without obligation.

Your hospital will procure Knox for your patients if you specify it by name.

KNOX GELATINE
(U.S.P.)

A SUPPLEMENTARY PROTEIN CONCENTRATE

SEND THIS COUPON FOR FREE BOOKLETS

KNOX GELATINE, Johnstown, N. Y. Dept. 408

Please send me ( ) copies of "Feeding Diabetic Patients—Young and Old." I understand there is no obligation.

Name.....

Address.....

Continued from page 40

Claiborne and Dr. Bernard P. Wolff received awards for the best written paper.

Chicago Eye, Ear, Nose & Throat College
Established 1897
231 W. Washington St., Chicago, Ill.
Practical postgraduate course in Ophthalmology and Otolaryngology.
Doctors admitted at any time for review and clinical observation.
Two residencies of one year each now available.
OSCAR B. NUGENT, M.D., Director

WANTED

Man with experience in the field of hospital equipment, preferably with some medical training, to sell Emerson Resuscitators in Southern Territory. Excellent earning for right man. Apply by letter to J. H. Emerson Company, 601 Central Union Building, Columbia, South Carolina.

Classified Advertisements

RATES for insertion in the Classified Column are as follows: $2.00 minimum, which includes the first 50 words; for each word in addition to the original 50 words, the charge is 3c.

WANTED: Well trained doctor under 40 years of age for general practice and some surgery to become an associate with a busy Oklahoma City general practitioner. Address inquiries to Dept. M-30, care JOURNAL.

REPRESENTATIVE WANTED—Salesman now calling upon the medical and dental professions, to carry profitable side-line offered by prominent medical publisher. Write fully to A. W. Volland, The C. V. Mosby Company, 3525 Pine Boulevard, St. Louis, Missouri.

WANTED—Experienced man as assistant resident; large traumatic and fracture service; American, Class A school; personal interview; salary commensurate with position; state race, religion and nationality. Address inquiries to Dept. D-2, care SOUTHERN MEDICAL JOURNAL, Birmingham, Alabama.

Dr. Charles O. Rainey, Camilla, on leave of absence from the Mitchell County Board of Health, is temporarily Area Medical Officer of the extracantonment area for Camp Stewart at Hinesville.

Dr. Irvin E. Simmons, formerly Director of the Nassau County Health Department in Fernandina, Florida, is Health Officer of Coffee County, with headquarters at Douglas.

Baldwin Memorial Hospital, Milledgeville, has appointed on its staff: Dr. O. C. Woods, Chief Surgeon and Director of Surgical Service; Dr. Chas. B. Fulghum, Chief and Director of Medical Service; and Dr. Harold W. Long, Senior Surgeon and Assistant Surgical Director. Dr. Richard Binion, Milledgeville, who was Chief Surgeon of the Hospital, has retired from active practice.

Crawford W. Long Memorial Hospital, Atlanta, has installed Dr. Shelley C. Davis as President of its staff, and elected Dr. W. L. Thomason, President-Elect; Dr. Calvin Weaver, Vice-President; and Dr. Joe H. Boland, Secretary.

Georgia Baptist Hospital, Atlanta, has elected on its staff: Dr. Geo. W. Fuller, Atlanta, President; Dr. Hal M. Davison, First Vice-President; Dr. Henry W. Minor, Second Vice-President; and Dr. Marion C. Pruitt, Secretary.

Walton County Hospital, Monroe, elected officers and trustees at its annual meeting in January, the staff consisting of: Dr. T. R. Aycock, Dr. E. S. Deaver, Dr. Lynn Huie, Dr. J. A. Pirkle and Dr. Phil R. Stewart, all of Monroe; Dr. W. D. Spearman and Dr. H. L. Upshaw, both of Social Circle; Dr. Chas. S. Floyd, Loganville; Dr. John Gerdine, Jersey; and Dr. W. M. Fambrough, Bostwick.

Dr. Frank K. Boland was elected Chairman of the Atlanta Chapter of the American Red Cross at its annual meeting in January.

Dr. W. E. Thomasson has been elected City Physician for Carrollton.

Dr. Thomas J. Charlton has been elected Superintendent of the Georgia Infirmary, Savannah.

Dr. Robert Brandt, Augusta, has moved to Cindinnati, Ohio.

DEATHS

Dr. Henry Turner Edmondson, Moultrie, aged 53, died January 18.
Dr. Selmer Dean Gausemel, Atlanta, aged 49, died January 18.
Dr. Walter H. Lott, Monroe, aged 60, died January 9.
Dr. James A. Otwell, Cumming, aged 58, died January 24 of heart disease.
Dr. William A. Palmour, Gainesville, aged 75, died February 1.
Dr. Hugo Robinson, Albany, aged 86, died January 8.
Dr. Obie Byron Walker, Bowman, aged 67, died February 5.
Dr. Tarpley William West, Shannon, aged 71, died January 24.

KENTUCKY

Pike County Medical Society has elected Dr. Henry Kaminiski, President; Dr. J. C. Preston, Vice-President; and Dr. F. H. Hodges, Secretary, all of Pikeville.

Union County Medical Society has elected Dr. J. W. Conway, Morganfield, President; Dr. Gordon B. Carr, Sturgis, Vice-President; and Dr. Bruce Underwood, Morganfield, Secretary.

Continued on page 44

To Assure Quick Dependable Response
Discriminating Physicians are Prescribing
the easily soluble
DUBIN AMINOPHYLLIN
THEOPHYLLINE-ETHYLENEDIAMINE
American Made from American Materials
H. E. DUBIN LABORATORIES
INCORPORATED
250 E. 43rd St. New York, N.Y.

The diagnostic value of any radiograph is, in the final analysis, dependent upon the specialized knowledge of the one who makes the interpretation. This is the reason why you should refer your patients to a competent radiologist.

Simple tumors of bone present characteristic radiographic appearances which permit of their identification by the experienced observer.

Malignant tumors of bone in the early stages present variable but characteristic radiographic features.

The recognition of one of these typical appearances should be followed by an x-ray examination of the lungs and pelvis for demonstration of possible metastases. The possibility that the bone lesion may be a metastasis from a primary carcinoma elsewhere should be considered.

No treatment should be administered until a complete radiographic record has been made.—RADIOLOGY, *33:* 494-5, 1939.

****The roentgen ray brought with it that same precision in the diagnosis and treatment of fractures that it contributed in the case of disease in bone or joint.*—J. BONE & JOINT SURG., *19:* 290, 1937.

EASTMAN KODAK COMPANY, ROCHESTER, N. Y.

World's largest manufacturer of radiographic and photographic materials

Continued from page 42

Woodford County Medical Society has elected Dr. W. C. McCauley, Versailles, President; Dr. S. J. Anderson, Midway, Vice-President; and Dr. George H. Gregory, Versailles, Secretary.

John Graves Ford Memorial Hospital, Georgetown, has elected Dr. H. V. Johnson, Chief of Staff; Dr. Ralph C. Lake, Assistant Chief of Staff; and Dr. F. M. Wilt, Secretary-Treasurer.

Dr. A. M. Lyon, Sandy Hook, has been appointed Director of Hospitals and Mental Hygiene by the Governor, succeeding Dr. J. G. Wilson, resigned.

The following Medical Reserve Officers have been called to service: Dr. Robert J. Griffin, Dr. Rufus C. Alley, Dr. Robert J. Downing and Dr. John H. Rompf, Lexington; Dr. Lee A. Dare, Lawrenceburg; and Dr. Robert L. Loftin, Cynthiana.

Dr. J. Mack Roberts and Miss Alma Dolan, both of Monticello, were married January 18.

Deaths

Dr. John R. Fairchild, Inez, aged 75, died January 14 of heart disease.

Dr. W. L. Gossett, Adairville, aged 61, died January 16.

LOUISIANA

The American Dermatological Association will hold its annual meeting in New Orleans, April 7-11. Dr. Harry R. Foerster, 208 East Wisconsin Avenue, Milwaukee, Wisconsin, is Secretary.

Bossier County Medical Society has elected Dr. D. C. McCuller, Bossier, President; Dr. W. F. Bell, Plain Dealing, Vice-President; and Dr. J. B. Hall, Benton, Secretary-Treasurer.

Third District Medical Society has elected Dr. J. J. Burdin, Lafayette, President; Dr. Henry Voorhies, Lafayette, Vice-President; and Dr. E. E. Guilbeau, Jr., Lafayette, Secretary-Treasurer.

Louisiana State University School of Medicine, New Orleans, has appointed Dr. Chester A. Stewart, formerly Clinical Professor of Pediatrics, University of Minnesota Medical School. Minneapolis, Professor and Head of the Department of Pediatrics. Other changes in the Medical School on a part-time basis are: Dr. Charles A. Bahn, Professor of Ophthalmology; Dr. Isidore Cohn, Professor of Surgery; Dr. Samuel Karlin, Clinical Assistant in Surgery; Dr. Eleazar R. Bowie, Clinical Professor of Radiology and Director of the Department of Radiology; and Dr. Frederick King Vaughan, Assistant Professor of Obstetrics and Gynecology.

Louisiana State Board of Health has been reorganized with Dr. John H. Musser, Professor of Medicine, Tulane University of Louisiana School of Medicine, New Orleans, as State Health Director. The following are members of the Board: Dr. Eugene B. Vickery, New Orleans, Chairman; Dr. Joseph E. Knighton, Shreveport, Vice-Chairman; and Dr. Paul King Rand, Alexandria. Dr. Robert H. Onstott, who has been serving as full-time executive officer of the Board, will continue in this capacity under the direction of Dr. Musser. Dr. Ford S. Williams, New Orleans, is Assistant Director of the State Board of Health.

Dr. Leon J. Menville, New Orleans, has been appointed a member of the State Board of Medical Examiners to succeed Dr. C. Grenes Cole, who is retiring from the Board. Dr. C. Walter Mattingly, a newly appointed member of the Board, succeeds Dr. M. H. Foster, of Alexandria, who is now the Director of the hospital at Pineville.

At the last annual session of the Lousiana Association of Health Officers the name was changed to the Louisiana Public Health Association. The following officers were elected: Dr. William W. Knipmeyer, Natchitoches, President, and Dr. Reuben Alec Brown, New Orleans, Secretary-Treasurer.

New Orleans Tuberculosis and Public Health Association of Louisiana has reelected Dr. W. H. Perkins, President, and elected Dr. A. J. Hockett, Second Vice-President; Dr. B. I. Burns, Director; Members of the Executive Committee: Dr. R. Alec Brown, Dr. Joseph A. Danna, Dr. Sydney Jacobs, Dr. M. E. Lapham, Dr. John H. Musser, Dr. I. L. Robbins, Dr. Robert A. Strong, Dr. Julius L. Wilson and Dr. J. O. Weilbaecher, Jr.

Dr. Marion S. Souchon, New Orleans, won the annual award for the most distinctive painting at the recent Mississippi Art Association exhibition in Jackson.

Dr. Rufus H. Alldredge, New Orleans, was recently certified by the American Board of Orthopedic Surgery.

Dr. Robert W. Faulk, Monroe, was guest of honor at the annual banquet of the Ouachita Parish Medical Society and was

Continued on page 46

You'll like THE STANDBY MODEL AS THOUSANDS DO!

Thousands of doctors and hospitals have shown their genuine approval of The STANDBY Model Baumanometer by buying it. Hundreds of hospitals have re-ordered. Many outstanding institutions have equipped throughout with it.

Three factors have influenced this widespread adoption—its unique practical features—its extreme convenience—its precise accuracy. Moreover, its EXACTILT Scale, utilized for the first time in any mercury-gravity bloodpressure instrument, is permanently set at the EXACT angle to insure maximum reading efficiency from standing or sitting position. Complete—it can be used quicker and easier than ever before. Compact—it is never in the way. Portable—it can be moved any place with the utmost ease.

When you purchase The STANDBY Model you have the satisfaction of knowing that you have an instrument developed with the specific needs of the doctor's office and hospital in mind . . . *a floor model* to render complete, efficient and economical bloodpressure service to a degree never before obtainable—in the office, private room, ward, operating room or out-patient department. Your dealer can supply you.

Get the facts and you will buy a Lifetime Baumanometer

Lifetime Baumanometer
STANDARD FOR BLOODPRESSURE

W. A. BAUM CO. Inc. NEW YORK
ORIGINATORS AND MAKERS OF BLOODPRESSURE APPARATUS EXCLUSIVELY

Buy with Confidence

Because the quality of medical gases cannot be determined except by accurate chemical analysis and these products are purchased and used sight unseen, CONFIDENCE must be placed in the Manufacturer. Back of the "Puritan Maid" label on every cylinder, identifying the products of the Puritan Compressed Gas Corporation, is a reputation earned through many years of service to the Profession, during which time we have grown to be one of the largest producers of these products in the world.

Puritan Mask and Bag complete **$7.00**

Has had widespread acceptance and is known for effective, economical administration of therapeutic gases. Write for Illustrated Booklet "Puritan Gas Therapy Equipment."

SEE YOUR PURITAN DEALER OR WRITE OUR NEAREST OFFICE

PURITAN COMPRESSED GAS CORP.

BALTIMORE BOSTON CINCINNATI ST. PAUL DETROIT
CHICAGO ST. LOUIS KANSAS CITY NEW YORK

• Puritan Dealers in Most Principal Cities •

"PURITAN MAID" GASES AND GAS THERAPY EQUIPMENT

VISIT WITH US AT . . . SOUTHEAST HOSPITAL CONFERENCE, April 17th-19th, in Jung Hotel at New Orleans—Space No. 15 . . . CAROLINAS-VIRGINIAS HOSPITAL CONFERENCE, April 24th-26th, in Textile Hall at Greenville, S. C. — Space No. 3.

HEMOSTASIS IN SURGERY DEMANDS

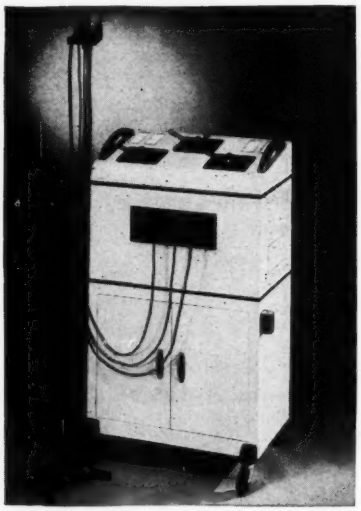
. . . . Clean Cutting

. . . . Control of Bleeding

Both hemostasis and clean cutting are accomplished in a single stroke when you use the new

Burdick SU-4

BLENDED CURRENT ELECTROSURGICAL UNIT



Blending of two currents in one provides the superior cutting qualities of the vacuum tube current with the coagulating ability of the spark gap current.

This new unit offers greater power for coagulation and smoother control for cutting, in addition to the ingenious Blended Current.

The BURDICK CORPORATION
MILTON, WISCONSIN

THE BURDICK CORPORATION SM 4-41
Milton, Wisconsin

I am interested in further information on the new BURDICK SU-4 Blended Current Electrosurgical Unit.

Dr. .....

Address .....

City ..... State .....

Continued from page 44

presented with a plaque in recognition of his more than fifty years' service in the community.

Dr. John G. Norris, Farmerville, has retired from active practice to take charge of the Union Parish Health Unit, a position he formerly held.

Dr. Charles W. Reid, Coushatta, has been appointed Director of the Red River Parish Health Unit.

Dr. Hilliard E. Miller, New Orleans, has been elected President of the American Gynecological Club, an organization with thirty American and ten foreign gynecologists. The next meeting will be held in New Orleans in February, 1942.

Dr. B. Bernard Weinstein, New Orleans, has been elected First Grand Chancellor of Phi Lambda Kappa, a national medical fraternity.

Dr. Marx D. Sterbcow, New Orleans, has been installed as President of the Young Men's Progressive Club.

Baptist Hospital, New Orleans, has elected for the year the following staff officers: Dr. E. A. Ficklen, President; Dr. H. C. Magee, Vice-President; Dr. E. Garland Walls, Secretary; and Dr. M. M. Hattaway, Treasurer.

Dr. Oliver P. Daly, former Superintendent of the Charity Hospital at Lafayette, has been appointed Superintendent of the Charity Hospital, New Orleans. Dr. J. O. Weilbaecher, Jr., and Dr. Charles B. Odom have been appointed Associate Superintendents in administrative capacities.

Deaths

Dr. S. F. Mioton, New Orleans, aged 68, was killed when hit by an automobile February 9.

MARYLAND

Medical and Chirurgical Faculty of Maryland will hold its next annual meeting at Baltimore, April 22-23.

Dr. Hugh H. Young, Baltimore, has been elected one of the corresponding members of the recently organized Venezuelan Urological Association.

MISSISSIPPI

Dr. Thomas L. Owings, Poplarville, Health Officer of Pearl River County, has been appointed Health Officer of Lafayette County, succeeding Dr. Murphy M. Sims, Oxford, who is in the military service.

Deaths

Dr. M. W. Robertson, Corinth, aged 52, died March 3.

MISSOURI

Bates County Medical Society has elected Dr. Charles A. Lusk, Jr., Butler, President; and Dr. A. L. Hanson, Appleton City, Secretary and Treasurer.

Dr. Evarts A. Graham, St. Louis, has been elected to the Royal Society of Sciences of Upsala, Sweden, an organization founded in 1710. This election is based on scientific merit in the member's chosen field. Dr. Graham was the only American in five new members elected recently.

Dr. Edward A. Doisy, Professor of Biological Chemistry at St. Louis University School of Medicine, has been awarded the William Gibbs Medal for isolating vitamin K by the Chicago Section of the American Chemical Society. The medal was presented in Chicago on May 23. This award is presented annually to a St. Louisan for outstanding contribution to the city or its institutions. Dr. Doisy also was given the St. Louis Award in 1939 for his isolation of vitamin K.

Dr. Mazyck P. Ravenel, Columbia, Editor and Editor-in-Chief of the *American Journal of Public Health* for the past sixteen years, has been made Editor Emeritus, and Dr. Harry Stoll Mustard, Director of the De Lamar Institute of Public Health of Columbia University, New York, has been appointed Editor.

Dr. Rexford L. Diveley, Kansas City, was elected Secretary of the American Academy of Orthopedic Surgeons at its annual meeting recently.

Deaths

Dr. John C. Bram, St. Louis, aged 67, died January 17.

Dr. Louis C. Boislinier, St. Louis, aged 80, died January 11 of laryngeal carcinoma.

Dr. Harvey E. Bowers, Galt, aged 64, died January 28.

Continued on page 48

PROGYNON-DH Tablets and Solution, for convenient and economical female hormone therapy *by mouth*: indispensable as adjunct to intensive therapy, or as complete therapy requiring moderate doses. Also in Ointment, Suppositories, and Nasal Spray.

The standard for most potent female sex hormone therapy . . . treatment with PROGYNON-B costs *less* than with preparations of the older types. It is the most advanced form of estrogen therapy and actually the most economical. **PROGYNON-B**

PROGYNON-DP

Follicular hormone ester (the dipropionate) for more prolonged therapeutic activity. PROGYNON-DH* is the free potent, primary follicular hormone, α-estradiol; PROGYNON-B,* the benzoate; and PROGYNON-DP,* the dipropionate.

*Trade-Marks Reg. U. S. Pat. off.

SCHERING CORPORATION • BLOOMFIELD • NEW JERSEY

Continued from page 46

Dr. Leander Cox, Springfield, aged 80, died January 7.
Dr. Robert L. Reber, St. Louis, aged 66, died January 20.

NORTH CAROLINA

Dr. Oscar L. Miller, Charlotte, was inducted into the presidency of the American Academy of Orthopedic Surgeons at its annual meeting in New Orleans, Louisiana, in January.

Dr. Russell L. Holman, Associate Professor of Pathology in the Medical School, University of North Carolina, has received a substantial research grant from the John and Mary R. Markle Foundation to aid in his studies on the role of hypersensitivity, diet and heavy metal injury in the production of arterial lesions.

Buncombe County Medical Society has installed Dr. Arthur C. Ambler, President, and elected Dr. G. Westbrook Murphy, President-Elect; Dr. Julian A. Moore, Vice-President; and Dr. Eugene M. Carr, Secretary, all of Asheville.

Dr. W. D. Farmer, Duke, is now with Dr. G. W. Banner, Greensboro, in practice of eye, ear, nose and throat.

Dr. Herman Franklin Eason and Miss Kathryn Amanda Scroggs, Raleigh, were married December 21.

Dr. Fleming Fuller, Kinston, and Miss Dorothy Barnes, Brenham, Texas, were married December 21.

Dr. Robert Richard Eason, Buena Vista, and Miss Mabel Nash, Blackstone, Virginia, were married December 21.

Dr. Colin Alexander Munroe and Miss Frances Foreman Crum, both of Durham, were married December 7.

DEATHS

Dr. C. E. Moore, Wilson, aged 87, died February 13.
Dr. James Marvin Wells, Middleburg, aged 65, died January 25.

OKLAHOMA

Dr. Everett S. Lain, Oklahoma City, has been appointed a Director of the National Board of the American Society for the Control of Cancer.

Pittsburg County Medical Society has elected Dr. William H. Kaiser, President; Dr. Thomas V. Norris, Vice-President; and Dr. E. D. Greenberger, Secretary.

Dr. Cyril E. Clymer, Oklahoma City, has been appointed a lieutenant colonel in the Army Reserve to serve as organizing director of a war-time evacuation hospital in Oklahoma City. He will select a staff of fourteen to function only in event of this country's entrance into the war.

SOUTH CAROLINA

Columbia Medical Society (Richmond County) has elected Dr. William Weston, Jr., President; Dr. S. W. Talbert, Vice-President; Dr. R. B. McNulty, Secretary; and Dr. W. A. Hart, Treasurer.

Greenville County Medical Society has installed Dr. C. C. Ariail, President, and elected Dr. J. Warren White, Vice-President and President-Elect; Dr. Keitt Smith, Secretary; and Dr. T. M. Northrop, Treasurer.

Florence County Medical Society has elected Dr. J. H. Stokes, Florence, President; Dr. W. E. Hicks, Sardis, Vice-President; and Dr. H. W. Herbert, Florence, Secretary-Treasurer.

Laurens County Medical Society has elected Dr. W. T. Pace, Gray Court, President; Dr. D. O. Rhames, Clinton, Vice-President; and Dr. J. L. Fennell, Waterloo, Secretary-Treasurer, re-elected.

The Carolinas-Virginias Hospital Conference will be held in Greenville, April 24-26, at the Textile Hall.

Dr. W. L. Pressly, Due West, President of the South Carolina Medical Association, has been elected to fill the unexpired term of the late Dr. E. A. Hines on the Executive Committee of the State Board of Health.

Dr. J. P. Young, Jr., formerly of Tennessee, has established his practice at North Charleston.

Dr. Charles A. Mobley, Orangeburg, was recently honored when the Medical Staff of the Tri-County Hospital at Orangeburg presented the institution wih a life-size oil painting of him in recognition of his services. Dr. Mobley's establishment of the Orangeburg Hospital twenty-one years ago provided the foundation from which grew the present modern Tri-County Hospital.

Continued on page 50

The New Emmert-Gellhorn Pessary

An improved device for treatment of inoperable uterine prolapse

For use in cases of inoperable uterine prolapse, this new pessary is offered as an improvement upon the well-known Gellhorn Pessary, long used with great success. The Emmert-Gellhorn Pessary is made of one solid piece of Neicomold, a synthetic material that may be boiled. The material is unbreakable and stays smooth in use since it is unaffected by the genital secretions. Neither does it affect or irritate the vaginal mucosa. The shape is approximately that of a mushroom, with the upper surface slightly depressed.

Instead of a solid stem, the Emmert-Gellhorn Pessary employs a stem having a hole drilled throughout its length. This offers the considerable advantage of drainage, preventing accumulation of dammed-up secretions. This permits fewer removals of the pessary for cleaning, of great benefit to the patient, particularly since many of those using this pessary are aged and find such frequent manipulation and visits to the physician a severe handicap.

The stem of the new pessary is ¼ inch shorter than that of the former pattern, and does not terminate in the knob formerly used. A slight hollowing of the stem near the end, however, allows easy grasp for removal. In weight, the Emmert-Gellhorn Pessary has the advantage of being considerably lighter. This decreased weight also adds to the comfort of the patient.

PRICE—JE5162 — Emmert-Gellhorn Pessary, Diameter 2 or 2½ inches, STATE SIZE, Each $2.25

SPECIAL SIZES: 2¼, 2¾ or 3-inch may be had on order at, each $2.75

A. S. ALOE COMPANY

1831 OLIVE STREET, ST. LOUIS, MO.

Constipation in Infancy

Laxatives

not needed to relieve

Constipation

when the daily feedings are prepared from milk properly modified with

Mellin's Food

Constipation in infancy probably commands the physician's attention more often than any other symptom that points to the need of readjusting a feeding formula.

Constipation is a common complaint and oftentimes is the real reason for a slow gain in weight, restless nights and a fretful, uncomfortable baby.

Infants fed on milk and water in proportions suitable for healthy babies of given age and weight with an amount of Mellin's Food to meet the carbohydrate requirement (*six to eight level tablespoons to the full day's mixture*) are seldom constipated.

Many physicians use Mellin's Food routinely in preparing bottle feedings, for they know from experience that regular stools of good consistency are characteristic of babies fed on milk properly modified with Mellin's Food. These physicians thus avoid much of the trouble associated with infant feeding.

Mellin's Food Co., Boston, Mass.

Samples sent to physicians upon request.

MELLIN'S FOOD: Produced by an infusion of Wheat Flour, Wheat Bran and Malted Barley admixed with Potassium Bicarbonate—consisting essentially of Maltose, Dextrins, Proteins and Mineral Salts.

Continued from page 48

Arrangements have been completed for the erection of a hospital in Dillon by the Roman Catholic Church in South Carolina.

Dr. Frank C. Owens, Columbia, was State Chairman for South Carolina for the Infantile Paralysis Campaign during the month of January.

The following officers of the Medical Reserve Corps have been called to active duty: Dr. John T. Cuttino, Columbia; Dr. George G. Durst, Greenville; Dr. Lucius B. Keels, Bishopville; Dr. Joseph H. King, Summerton; Dr. Francis C. McLane, Abbeville; Dr. Harold L. Poole, Spartanburg; Dr. Keith Sanders, Kingstree; and Dr. Edwin M. Sirlin, Moultrie.

Dr. A. J. Buist, Jr., Charleston, has been called in the Naval Reserve Corps.

Dr. Donald S. Tarbox, formerly of Asheville, North Carolina, plans to reside permanently at Mauldin and will continue his practice there.

Dr. R. K. Brown, Greenville, has become a member of the American College of Chest Physicians.

Dr. Jeff Chapman, now residing in Walterboro, has taken over the work of Dr. Geo. C. Brown, who has been called to military service.

Dr. George Laub, formerly of Columbia, is now connected with the Johnston Memorial Hospital at Hemmingway.

Dr. R. W. Ball is Commanding Officer of the Medical Detachment, 107th Separate Battalion, Coast Artillery (AA) and is now stationed at Camp Stewart, Hinesville, Georgia, in the capacity of Battalion Surgeon. Dr. Hilla Sheriff has been appointed to take over the Maternal and Child Health Division of the State Board of Health until the return of Dr. Ball.

Dr. J. A. Dillard, Columbia, has been elected Vice-President of the local Emory University Alumni Chapter.

TENNESSEE

Henry County Medical Society has elected Dr. A. F. Paschall, Puryear, President; Dr. Elroy Scruggs, Paris, Vice-President; and Dr. R. Graham Fish, Paris, Secretary-Treasurer.

A diagnostic clinic and psychiatric hospital, an addition to the John Gaston Hospital, Memphis, teaching hospital of the University of Tennessee College of Medicine, is to be built at a cost of $450,000. It will have six floors, four to be used as an outpatient department for the Johns Gaston Hospital, and two for a fifty-bed psychiatric hospital. All patients admitted to the Western State Hospital at Bolivar will enter the psychiatric hospital for diagnosis, and selected cases will be kept there for treatment. Medical students will be rotated through the psychiatric hospital as in other departments.

Dr. Ernest W. Goodpasture, Nashville, was elected a Vice-President of the American Association for the Advancement of Science and Chairman of the Section on Medical Sciences at the annual midwinter meeting in Philadelphia, Pennsylvania.

The Learline Reaves Sanatorium, near Greenville, valued at $40,000 fully equipped, has been presented by W. Harvey Reaves to the East Tennessee Tuberculosis Association as a gift in memory of his daughter, who died five years ago of tuberculosis.

Dr. John R. Thompson, Jr., Jackson, has been appointed a member of the State Public Health Council for three years.

Dr. James P. Moon, Dyersburg, Health Officer of Dyer County, has been appointed Health Officer of Franklin County to succeed the late Dr. Victor J. Ganey.

Deaths

Dr. J. S. Campbell, Lebanon, aged 78, died February 3.
Dr. K. S. Howlett, Franklin, aged 79, died January 22.
Dr. J. M. Oliver, Portland, aged 54, died January 11.
Dr. G. L. Williamson, Jackson, aged 60, died January 6.

TEXAS

Austin-Waller Counties Medical Society has elected Dr. Malcolm A. Jones, Hempsted, President; Dr. Winston S. Thiltgen, Bellville, Vice-President; and Dr. Otto E. Steck, Bellville, Secretary-Treasurer.

Bexar County Medical Society has elected Dr. Frank N. Hag-

Continued on page 52

SANDOZ

CALCIUM ACTION combined with BROMINE SEDATION

CALCIBRONAT

CALCIUM-BROMIDO-GALACTOGLUCONATE

A new organic salt with the high calcium ratio—1 Ca : 2 Br
Less danger of bromism — Palatable — Well tolerated

EFFERVESCENT TABLETS: Tins - 10 and 50
GRANULES (non-effervescent): Tins - 100 and 500 Gm.
AMPULES: 10 cc.
BOXES: 5, 20 and 100

Literature and samples on request

SANDOZ CHEMICAL WORKS, Inc. • New York, N. Y.

SERENIUM

chemotherapeutic agent for genito-urinary infections

SERENIUM is an antiseptic azo dye of high purity and uniformity, especially prepared for the oral treatment of genito-urinary infections.

With a normal fluid intake Serenium, in a dosage of one tablet three times daily, imparts an orange or reddish color to acid urine and its concentration, about 1 to 5000, has a bacteriostatic effect on pyogenic organisms. Concentrations of Serenium as low as 1 part in 20,000 of urine are also reported to be bacteriostatic.

Serenium is of value in genito-urinary practice, particularly in conditions where there is idiosyncrasy to the sulfonamide drugs or where their use is for other reasons not feasible. It may also be employed advantageously between courses of mandelic acid therapy.

Serenium is effective in either acid or alkaline urine but more effective where the urine is acid. It has low toxicity, an adequate margin of therapeutic safety and a wide compatibility with other drugs which may be administered in genito-urinary infections.

"Serenium" is a trade-mark of E. R. Squibb & Sons.

Free Trial Package on Request

Serenium has a wide field of usefulness in treating genito-urinary infections. A request on your professional card or letterhead will bring you a generous trial package.

Mail the coupon—NOW!

E·R·Squibb & Sons

MANUFACTURING CHEMISTS TO THE MEDICAL PROFESSION SINCE 1858

NEW YORK

E. R. SQUIBB & SONS, SMJ4-41
Professional Service Department,
745 Fifth Avenue, New York, N. Y.

Gentlemen: Attached hereto is my professional card or letterhead. Please send me, without obligation, literature and sample of Serenium.

Name .....

Street .....

City ..... *State* .....

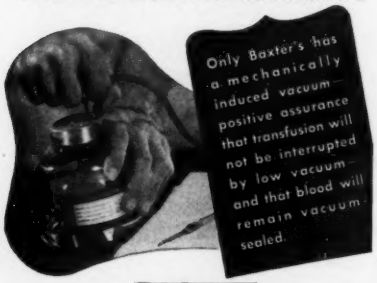
BAXTER
PIONEER "READY-TO-USE" SOLUTIONS IN VACOLITERS

A Complete LINE
NOT JUST
THE Best Sellers

A complete range of solutions in types, percentages and sizes to meet every recognized professional requirement. Sodium Chloride, Dextrose, Ringer's, Lactate-Ringer's, Acacia, 1-6 Molar Sod. Lactate, Sulfanilamide, Sodium Citrate.

★

TRANSFUSO-VAC
PROVIDES DEPENDABLE VACUUM FOR TRANSFUSIONS


Only Baxter's has a mechanically induced vacuum — positive assurance that transfusion will not be interrupted by low vacuum — and that blood will remain vacuum-sealed.

Products of
BAXTER LABORATORIES
Glenview, Ill.; College Point, N. Y.;
Glendale, Cal.; Toronto, Canada; London, England
Produced and distributed in the
Eleven Western States by
DON BAXTER, INC., Glendale, Cal.
Distributed East of the Rockies by
AMERICAN HOSPITAL SUPPLY CORPORATION
Chicago New York

Continued from page 50

gard, President; Dr. E. M. Sykes, Vice-President; Dr. W. W. Bondurant, Jr., Secretary, reelected; and Dr. C. B. Alexander, Treasurer, reelected.

Brooks-Duval-Jim Wells Counties Medical Society has elected Dr. J. H. Thomas, Freer, President; Dr. M. H. Appel, Alice, Vice-President; and Dr. Thelma E. Frank, Benavides, Secretary-Treasurer.

Caldwell County Medical Society has elected Dr. M. W. Pitts, President; Dr. Pruett Watkins, Vice-President; and Dr. J. T. O'Banion, Secretary-Treasurer.

Cherokee County Medical Society has elected Dr. M. S. Wheeler, Rusk, President; Dr. W. A. McDonald, Alto, Vice-President; and Dr. T. H. Cobble, Rusk, Secretary-Treasurer, reelected.

Dallas County Medical Society has elected Dr. Homer Donald, President; Dr. J. N. McLeod, Vice-President; Dr. W. W. Fowler, Secretary-Treasurer, reelected.

Dawson-Lynn-Terry-Gaines-Yoakum Counties Medical Society has elected Dr. L. D. Richards, Seminole, President; Dr. Emil Prohl, Tahoka, Vice-President; and Dr. Wayne C. Hill, Tahoka, Secretary-Treasurer.

Gray-Wheeler Counties Medical Society has elected Dr. Clifton High, Pampa, President; Dr. Malcolm Brown, Pampa, Vice-President for Gray County; Dr. J. W. Gooch, Shamrock, Vice-President for Wheeler County; and Dr. G. R. Walker, Wheeler, Secretary, reelected.

Hardeman-Cottle-Motley-Foard Counties Medical Society has elected Dr. J. J. Hanna, Quanah, President; Dr. T. D. Frizzell, Quanah, Vice-President; and Dr. A. C. Hughes, Roaring Springs, Secretary-Treasurer.

Hunt-Rockwall-Rains Counties Medical Society has elected Dr. W. M. Dickens, President; Dr. E. T. Crim, Vice-President; and Dr. M. L. Wilbanks, Secretary-Treasurer, reelected.

Hutchinson-Carson Counties Medical Society has elected Dr. L. M. Draper, President; Dr. L. E. Petty, Vice-President; and Dr. W. M. Stephens, Secretary, all of Borger.

Jefferson County Medical Society has elected Dr. T. A. Fears, Beaumont, President; Dr. W. Price Killingsworth, Port Arthur, Vice-President; and Dr. George L. Butler, Beaumont, Secretary-Treasurer.

Liberty-Chambers Counties Medical Society has elected Dr. B. L. Jordan, Daisetta, President; Dr. Walter Leggett, Cleveland, Vice-President; and Dr. E. J. Tucker, Liberty, Secretary-Treasurer.

Nueces County Medical Society has elected Dr. C. P. Jasperson, President; Dr. G. Turner Moller, Vice-President; and Dr. C. J. Connor, Secretary-Treasurer, all of Corpus Christi.

Palo-Pinto-Parker Counties Medical Society has elected Dr. Leo N. Roan, Weatherford, President; Dr. Ben L. McCloud, Graford, Vice-President; and Dr. J. Edward Johnson, Mineral Wells, Secretary-Treasurer.

Titus County Medical Society has elected Dr. John M. Ellis, President; Dr. T. R. Bassett, Vice-President; and Dr. William A. Taylor, Secretary-Treasurer, all of Mount Pleasant.

Texas Ophthalmological and Otolaryngological Society, at its annual meeting in Fort Worth in December, elected Dr. Everett L. Goar, Houston, President; Dr. Burbank P. Woodson, Temple, and Dr. Phocian W. Malone, Big Spring, Vice-Presidents; and Dr. Daniel Brannin, Dallas, Secretary, reelected.

Joanna McClelland Memorial Hospital Staff, Waco, has elected Dr. Wilson Crostwait, Chief of Staff; Dr. M. B. Aynesworth, Assistant Chief of Staff; and Dr. Clayton J. Traylor, Secretary.

City-County Hospital Staff, Fort Worth, has elected Dr. Heywood Davis, Chairman; Dr. DeWitt Neighbors, Vice-Chairman; and Dr. Mal Rumph, Secretary. Dr. Sim Hulsey and Dr. Jarrell Bennett were chosen new members of the Executive Board.

Municipal Hospital Staff, Ennis, has elected Dr. A. J. Cox, Chairman, reelected; Dr. J. Lawrence Clark, Vice-Chairman; and Dr. John M. Chapman, Secretary.

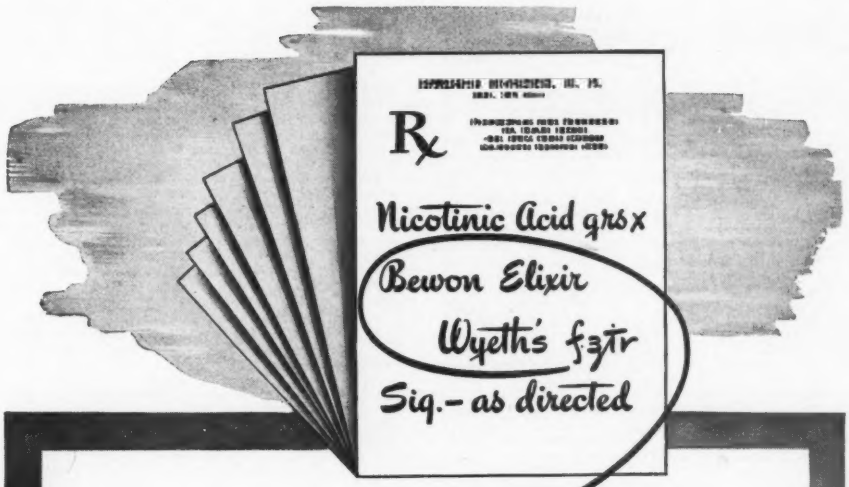
Bethea Hospital Staff, Wichita Falls, has elected Dr. Bailey R. Collins, President; Dr. J. A. Heymann, Vice-President; Dr. J. A. Little, Secretary; and Dr. Robert Hargrave, Assistant Secretary. Other members of the Executive Board are Dr. C. H. Bishop, Dr. J. E. Kanatser and Dr. G. T. Singleton.

Hendrick Memorial Hospital Staff, Abilene, has elected Dr. W. V. Ramsey, Chairman; Dr. B. F. Rhodes, Vice-Chairman; and Dr. E. E. Middleton, Secretary. Other members of the Board are Dr. Frank Hodges, Dr. Jack Estes, Dr. L. F. Johnson, Jr., Dr. J. N. Burditt and Dr. W. B. Adamson.

Harris Memorial Hospital, Fort Worth, has elected Dr. Judge M. Lyle, Chairman; Dr. A. I. Goldberg, Vice-Chairman; and Dr. Theron H. Funk, Secretary.

Methodist Hospital Staff, Houston, has elected Dr. L. L. D

Continued on page 54



This vehicle *stimulates the appetite*

Wyeth's BEWON* ELIXIR is an excellent vehicle for many medicaments. It is compatible with most drugs.

Standardized to contain 500 International Units of Vitamin B_1 (thiamin chloride) per ounce, BEWON ELIXIR stimulates the appetite and is indicated in Vitamin B_1 deficiencies.

Supplied in pint and gallon bottles

*Reg. U. S. Pat. Off.

John Wyeth and Brother Incorporated PHILADELPHIA

Continued from page 52

Tuttle, President; Dr. James Greenwood, President-Elect; Dr. W. S. McDaniel, Vice-President; and Dr. B. B. Smith, Secretary.

Jefferson Davis Hospital Staff, Houston, has elected Dr. T. R. Hannon, President; Dr. P. H. Scardino, Vice-President; Dr. John H. Wootters, Secretary, reelected; Dr. Fred Smith, Chairman of Surgical Division; and Dr. E. R. Seale, Chairman of Medical Division.

Cleveland Hospital, the first hospital for the City of Cleveland, was formally opened January 2. The staff is composed of Dr. Walter Leggett and his associates, Dr. Clell Holland and Dr. M. K. Leggett, of Houston.

McLennan County Tuberculosis Clinic, Waco, was opened January 9 at the Joanna McClelland Memorial Hospital and will be operated under the direction of the McLennan County Tuberculosis Association and under the supervision of Dr. D. D. Wall, Dr. B. M. Aynesworth, Dr. Ralph Coffelt, Dr. Horace Trippett and Dr. C. G. Traylor, all of Waco.

Texas Radiological Society held its twenty-eighth annual meeting as a memorial to the late Dr. W. G. McDeed, of Houston, at Sherman, January 18. The following officers were elected: Dr. M. H. Glover, Wichita Falls, President; Dr. G. D. Carlson, Dallas, President-Elect; Dr. Palmer E. Wigby, Dallas, First Vice-President; Dr. Tom Bond, Fort Worth, Second Vice-President; and Dr. L. W. Baird, Temple, Secretary-Treasurer.

Dr. Fred Lummis, Houston, was recently appointed Chief of Staff of the Hermann Hospital, Houston, for the third successive year.

Dr. T. C. Strickland, Greenville, has been doing postgraduate study in eye, ear, nose and throat work in New Orleans, Louisiana.

Dr. Fred N. Felder, Palestine, has been reappointed County Health Officer of Anderson County.

Dr. Bruce Hay, Dallas, has been appointed Assistant Medical Officer of the venereal disease clinic at Parkland Hospital, succeeding Dr. T. L. Shields, who resigned to take an internship.

Dr. T. J. Pennington, Nacogdoches, has been named County Health Officer of Nacogdoches for a two-year term.

Dr. Sam Ellis and Dr. E. J. Arendt, San Antonio, have been appointed part-time physicians in the City Health Department to replace Dr. Ralph C. Letter, full-time physician, now on duty with the U. S. Army.

VIRGINIA

The fifteenth annual spring graduate course in ophthalmology and otolaryngology will be presented by the Gill Memorial Eye, Ear and Throat Hospital, Roanoke, April 7-12.

Neuropsychiatric Society of Virginia has elected Dr. W. Gayle Crutchfield, President; Dr. Howard R. Masters, Vice-President; and Dr. Edward H. Williams, Secretary-Treasurer, reelected, all of Richmond.

Richmond Pediatric Society has elected Dr. Louise Fry Galvin, President; Dr. T. Stanley Meade, Vice-President; and Dr. Herman W. Farber, Secretary-Treasurer.

The annual spring postgraduate clinics of the Medical College of Virginia will be held in Richmond in conjunction with the Stuart McGuire Lectures, which will be delivered by Dr. Alfred Blalock, Vanderbilt University School of Medicine, Nashville, Tennessee, on April 24 and 25.

The twenty-seventh annual postgraduate clinic of the University of Virginia Department of Medicine will be held April 11.

Children's Memorial Clinic, Richmond, has elected Dr. Charles J. Outland, President; Dr. Henry W. Decker, Vice-President; and Dr. Harvie DeJ. Coghill, Director of the Clinic, Secretary. Dr. Manfred Call, III, was reelected as a member of the Board for a term of three years.

The Radford Community Hospital, with a capacity of about thirty beds, was opened in February. The Board of Directors is Dr. J. J. Giesen, Dr. T. L. Gemmill, Dr. H. L. Dean, Dr. H. D. Fitzpatrick, Dr. E. G. Hall and Dr. J. L. Early, of Radford; Dr. A. M. Showalter, Dr. R. H. Grubbs, Dr. R. M. DeHart and Dr. E. P. Ambrose, of Christianburg. Dr Giesen is President of the Board.

Richmond Academy of Medicine has elected the following officers of the Section on the History of Medicine: Dr. Marvin Pierce Rucker, Chairman; Dr. William Lowndes Peple, Vice-Chairman; and Dr. Alexander Stephens Graham, Secretary-Treasurer.

Continued on page 56

LaMOTTE BLOOD CHEMISTRY SERVICE

NEW and IMPROVED
LaMOTTE FALLING DROP DENSIOMETER
(Two Models)

For determining blood proteins, albumin-globulin ratio and specific gravity of body fluids. These units are produced exclusively with the cooperation of H. G. Barbour and W. F. Hamilton, and approved by them.

This outfit is now available in two models—the larger model comes complete for $65 and the small model at $35. Prices F.O.B. Towson, Md.

Send for complete information.

This Service includes a series of similar outfits for conducting the following accurate tests: Blood Sugar, Blood Urea, Sulfathiazol, Sulfapyridine and Sulfanilamide in Blood. Icterus Index, Phenolsulphonphthalein Urine pH, Blood pH, Gastric Acidity, Calcium-Phosphorus, Blood Bromides, Blood Proteins, Urinalysis.

LaMOTTE CHEMICAL PRODUCTS CO., Dept. S, Towson, Baltimore, Maryland

DR. MOODY'S SANITARIUM

SAN ANTONIO, TEXAS

315 Brackenridge Avenue **Phone: Fannin 5522**

For Nervous and Mental Diseases, Drug and Alcohol Addiction and Nervous Invalids Needing Rest and Recuperation

Established 1903. Strictly ethical. Location delightful summer and winter. Approved diagnostic and therapeutic methods. Seven buildings, each with separate lawns, each featuring a small separate sanitarium, affording wholesome restfulness and recreation, in doors and out doors, tactful nursing and homelike comforts.

G. H. MOODY, M.D.
Founder

J. A. McINTOSH, M.D., F.A.C.P.
Superintendent

VEGEX AND VEGEX-VITAFOOD DRIED BREWERS YEAST FOR THE COMPLETE VITAMIN B COMPLEX

"The simplest definition of the vitamin B complex is that it is an assemblage of the water-soluble vitamin factors present in yeast." (The Lancet, November 2, 1940, page 558.)

Vegex, the autolyzed extract of grain grown brewers' yeast, has long been the standard for the complete vitamin B complex in important medical centers throughout the world as well as in private practice.

Thiamin, riboflavin, B_6, nicotinic acid and the components of the "filtrate factor" are all contained naturally within the yeast cell. The autolyzing or self-digestion process breaks open the yeast cell, thereby making the contents of the cell more readily available.

Autolyzing the yeast frees or develops a potent anti-anemic principle which has been identified as the extrinsic factor. There have been over sixty published reports in medical literature on the successful use of Vegex in the anemias.

When the vitamin B complex is required it should be remembered that there is no more potent or complete source than brewers' yeast or its extracts like Vegex.

In their article on "Riboflavin Deficiency in Man" (*New England Journal of Medicine*, 221:921-926, 1939), Jolliffe, Fein and Rosenblum state that they found Vegex relieves both riboflavin deficiency and pellagra.

Easily Administered

Vegex is in paste form. The meat-like flavor is characteristic of autolyzed yeast proteins but Vegex is meat-free. A scant teaspoonful dissolved in a cup of hot water makes an instant bouillon. Or Vegex may be added to other soups, vegetables, milk, etc.

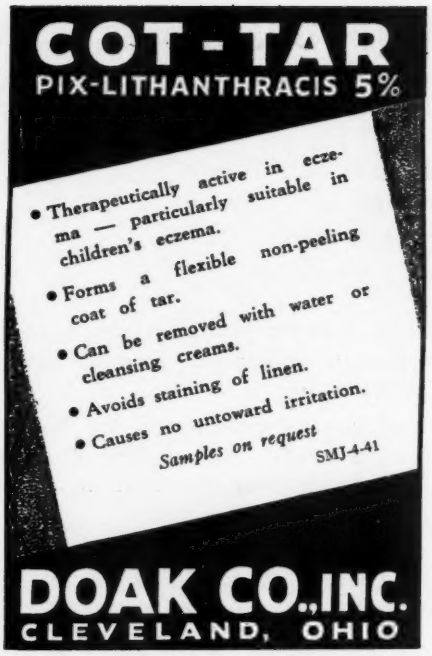
Vegex-Vitafood Dried Brewers Yeast

Over five million pounds of Vegex-Vitafood Dried Brewers' Yeast have gone into the South for the successful treatment of pellagra. Few, if any, products have been kept so closely under the direction of physicians and health officers.

●

Samples for clinical or professional use will be sent on request.

VITAMIN FOOD CO., INC. 122 Hudson St. New York, N. Y. **VEGEX, INCORPORATED**


COT-TAR
PIX-LITHANTHRACIS 5%
• Therapeutically active in eczema — particularly suitable in children's eczema.
• Forms a flexible non-peeling coat of tar.
• Can be removed with water or cleansing creams.
• Avoids staining of linen.
• Causes no untoward irritation.
Samples on request
SMJ-4-41
DOAK CO., INC.
CLEVELAND, OHIO

Laboratory and X-Ray Course

IS NOW TEN MONTHS IN DURATION

Supplemented by Six Months' Practical Work in a Hospital Laboratory, comprising 16 months in all.

COURSE INCLUDES:

Clinical Pathology
Bacteriology
Blood and Urine Chemistry
Hematology
Tissue Sections, Frozen and Paraffin
Serology
Parasitology
Basal Metabolism
Electrocardiography
Roentgenology

A corps of experienced teachers plus completely equipped teaching laboratories covering 3100 square feet.

Write for new catalogue (1940)

Gradwohl School of Laboratory and X-Ray Technique

3514 Lucas Avenue, St. Louis, Missouri
R. B. H. Gradwohl, M.D., Director

Continued from page 54

Mary Washington Hospital, Fredericksburg, has received from an anonymous donor a gift of $20,000.

Richmond Tuberculosis Association has reelected Dr. T. Dewey Davis and Dr. Kinloch Nelson, Vice-Presidents; Dr. R. C. Bryan as an honorary Vice-President, and Dr. S. A. Anderson, Dr. Emily Gardner and Dr. D. Talley, Directors.

Dr. W. W. Butzner, Fredericksburg, has been named on the City Council as a member of the City Health Board to fill the vacancy caused by the resignation of Dr. Earle R. Ware. Dr. Thomas S. Payne, City Health Officer, is also a member of the Board.

Dr. L. S. Early, Petersburg, was honored at the annual banquet meeting of the Petersburg Medical Faculty by being presented with a loving cup for having practiced medicine in Petersburg longer than any other man living.

Dr. J. Bolling Jones, Petersburg, was presented a loving cup at the regular meeting of the Fourth District and Southside Virginia Medical Society for the unique place he has made for himself in his contact with patients and doctors during his more than forty years of practice.

Dr. H. L. Hamilton, formerly of Goshen, is now with the Hercules Powder Company in Radford in charge of Hospital Unit Number 3.

Dr. W. W. Wilkinson, LaCrosse, has been reelected President of the Board of Directors of the Bank of LaCrosse; Dr. D. C. Boatwright, a Director of the Bank of Marion; and Dr. J. D. Buchanan a Director of the Marion National Bank. Dr. J. H. Mapp, Buena Vista, has been reelected President and a Director of the Peoples Bank.

Dr. Porter P. Vinson, Richmond, announces removal of his offices from Medical Arts Building to the new Medical College of Virginia Hospital Building.

Dr. Charles D. Smith, formerly of Richmond, is now located at Roanoke with offices in the Medical Arts Building. He is associated with Dr. Charles H. Peterson and Dr. Allen Barker, with practice limited to radiology.

Dr. A. L. Carson, Richmond, who has been acting as Head of the Bureau of Maternal and Child Health of the State Health Department since the retirement of Dr. B. B. Bagby on July 1, has been appointed as full-time Director of that Bureau.

Dr. J. B. Porterfield, Richmond, recently State Epidemiologist in the Bureau of Communicable Diseases, has been appointed Director of the Bureau of Industrial Hygiene.

Dr. Thomas E. Painter, formerly of Williamsburg, has located in Radford, where he is associated in general practice with Dr. T. L. Gemmill.

Dr. Walter J. Rein, recent associate in ophthalmology of the late Dr. Emory Hill, announces the continuation of his practice at the same address in the Professional Building, Richmond.

Dr. Walter B. Martin, Norfolk, has been appointed by the Governor a member of the Hampton Roads Regional Defense Council, and Dr. D. S. Divers, of Pulaski, to the Radford Area Defense Council.

Dr. Richard C. Potter, Marion, has been called into active duty at the Army Medical Center, Walter Reed General Hospital, Washington, D. C.

Dr. George Craddock Barksdale and Miss Mary Spencer Jack, both of Lynchburg, were married February 1.

Dr. Wm. Fitzgerald Cavedo and Miss Edith Farline Mann, both of Richmond, were married February 12.

Deaths

Dr. Edward Anderson Holmes, Marion, aged 68, died February 4.

Dr. William Elbert Jennings, Danville, aged 55, died January 26 of a heart attack.

Dr. Thomas Bernard Latane, Stevensville, aged 69, died February 18.

Dr. Moses Hoge Tredway, Emporia, aged 45, died February 8.

Dr. Joseph Augustus White, Richmond, aged 92, died February 16.

WEST VIRGINIA

American Surgical Association will hold its next meeting at White Sulphur Springs, April 28-30.

Dr. Martin Frank Wright, Burlington, was honored at a recent meeting of the Potomac Valley Medical Society in Romney, the meeting being held in his honor celebrating his fiftieth anniversary of medical practice. He was then President of the Society.

Deaths

Dr. Mortimer Daniel Cure, Weston, aged 73, died January 1.

ONLY VI-SYNERAL SUPPLIES CALCULATED POTENCIES OF VITAMINS *AND* MINERALS FOR EACH AGE GROUP

- **VITAMIN AND MINERAL DEFICIENCIES ARE USUALLY *MULTIPLE*.**
- **THE VITAMIN-MINERAL NEEDS OF AN ADULT DIFFER FROM THOSE OF AN INFANT —OR THE MIDDLE-AGED.**
- VI-SYNERAL,* the original multiple vitamin-mineral concentrate, is the only ethical product supplying specially balanced potencies for each age group: (1) INFANTS and CHILDREN, (2) ADOLESCENTS, (3) ADULTS, (4) EXPECTANT and NURSING MOTHERS, (5) SPECIAL GROUP (Middle-aged and Aged Patients).

VI-SYNERAL gives your patients an individualized dosage of vitamins and minerals in Funk-Dubin balances. Each VI-SYNERAL product contains VITAMINS A, B_1, B_2(G), C, D, E, and other B Complex factors, together with essential MINERALS: calcium, phosphorus, iron, copper, iodine, manganese, magnesium and zinc.

Special Group VI-SYNERAL contains higher potencies of VITAMINS B_1, B_2, B_6, Nicotinic Acid and C.

Literature describing each VI-SYNERAL product potency, together with sample, sent upon request.

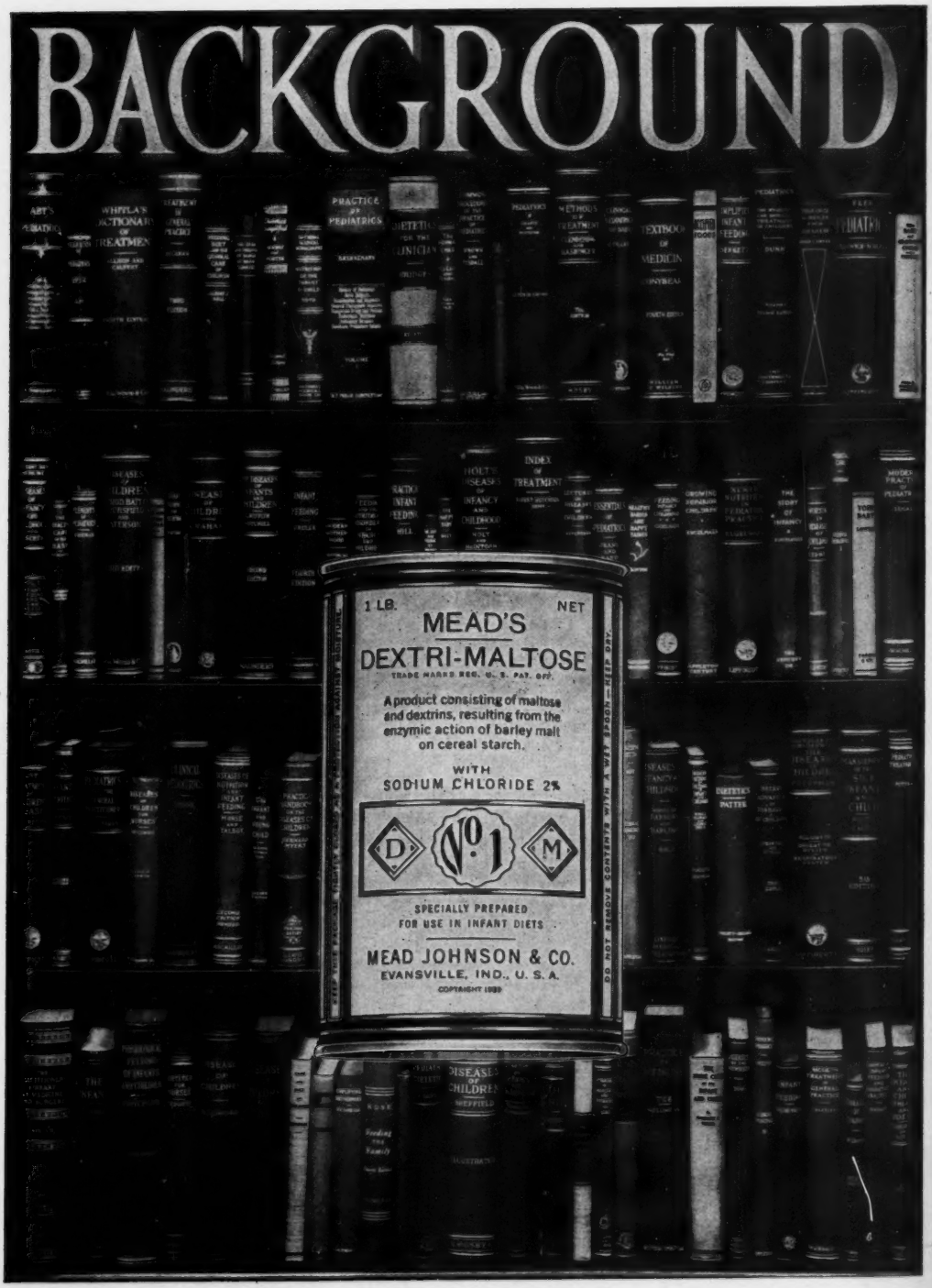
U. S. VITAMIN CORPORATION, 250 East 43rd Street, New York, N. Y.

*Trade Mark Reg. U. S. Pat. Off.

VITAMINS ALONE ARE NOT ENOUGH!

BECAUSE VITAMINS ARE BETTER UTILIZED WITH MINERALS VI-SYNERAL SUPPLIES BOTH!

BACKGROUND



THE use of cow's milk, water and carbohydrate mixtures represents the one system of infant feeding that consistently, for three decades, has received universal pediatric recognition. No carbohydrate employed in this system of infant feeding enjoys so rich and enduring a background of authoritative clinical experience as Dextri-Maltose.

Are the Neuritic Symptoms of Pregnancy *due to a deficiency of vitamin B_1 (thiamine)?*

SUCH common neuritic symptoms of pregnancy as pains in arms and legs, muscle weakness, and (less frequent but more serious) paralysis of the extremities may result from a shortage of antineuritic vitamins, recent investigations appear to show. Although neuronitis of pregnancy has long been considered a toxemia, no toxins have ever been identified.

Clinical observations of Strauss and McDonald lead to the conclusion that the condition is a dietary deficiency disorder similar to beriberi, caused by lack of vitamin B_1. They report recovery in their cases receiving this therapy, including dried brewers' yeast.

Hyperemesis as Cause of Avitaminosis

Wechsler observes that all cases of polyneuritis of pregnancy recorded in the literature were preceded by long periods of severe vomiting. "It would seem," he adds, "that because of actual starvation these patients suffered from avitaminosis and consequent neuritis," a view likewise held by Hirst, Luikart, and Gustafson. Plass and Mengert observe that the practice of giving high carbohydrate feedings for hyperemesis gravidarum is still more likely to cause avitaminosis.

Dried brewers' yeast, as it is far richer than any other food in vitamin B_1 (thiamine), is being used with benefit both in the prevention and treatment of polyneuritic symptoms of pregnancy. Lewy found that additions of yeast to the diet reduced electric irritability of the peripheral nerves and brought clinical improvement. Vorhaus states that he and his associates, after administering large amounts of vitamin B_1 (thiamine) to 250 patients having various types of neuritis, including that of pregnancy, observed in about 90% of cases "varying degrees of improvement, i.e., from partial relief of pain to complete disappearance of all symptoms."

Need for Vitamin B_1 (thiamine) in Lactation

Evans and Burr, Hartwell, Sure and co-workers, and Macy *et al* are among numerous authorities who find that the nursing mother also needs a supplement of vitamin B_1 (thiamine) from 3 to 5 times the normal requirement. It is accepted that during pregnancy and lactation the requirement for vitamin G (riboflavin) is increased.

Consisting of nonviable yeast, Mead's Brewers Yeast Tablets offer not less than 50 International vitamin B_1 (thiamine) units and 50 Sherman vitamin G (riboflavin) units per gram (20 International units of vitamin B_1 and 20 Sherman units of vitamin G per tablet).

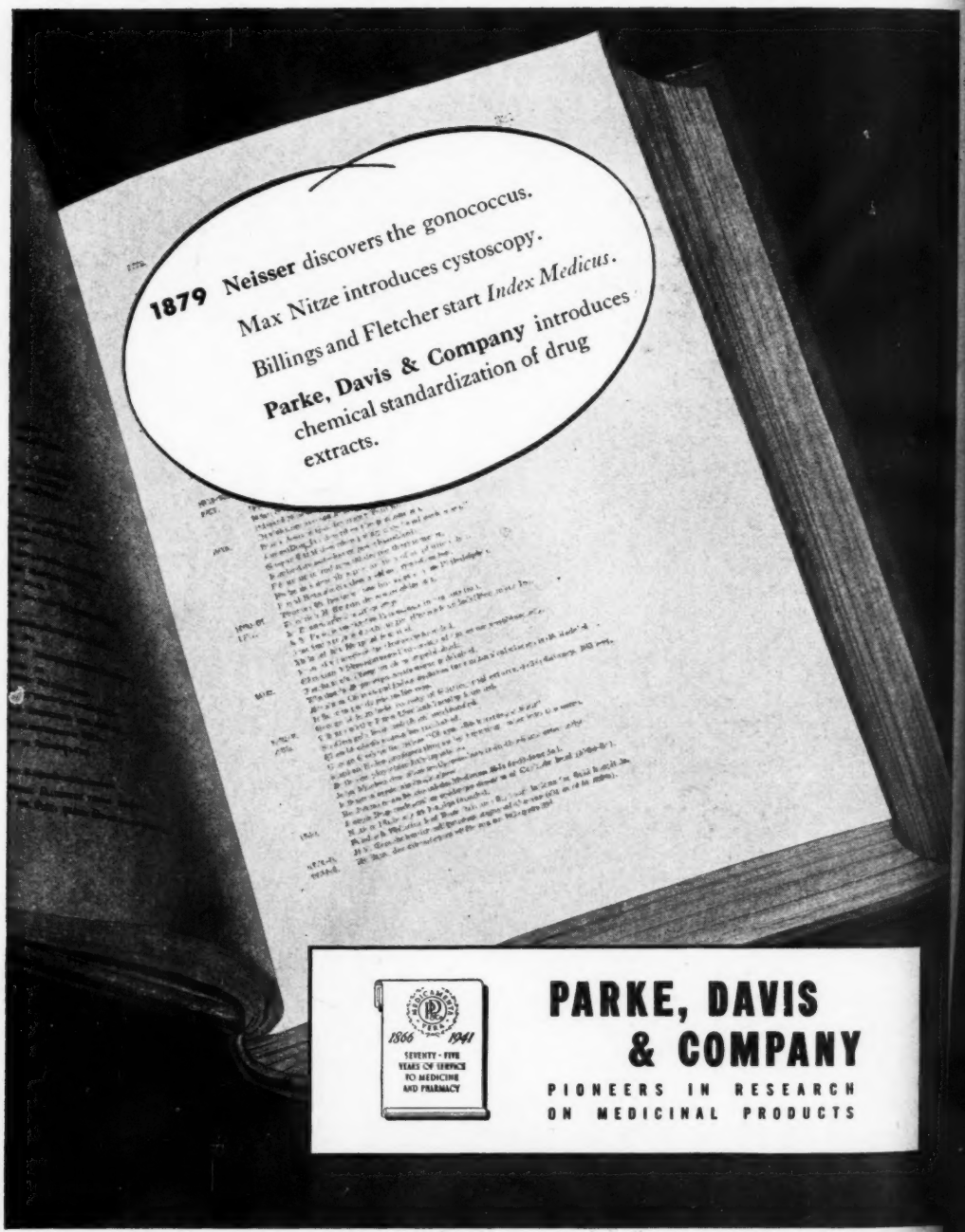
Supplied in bottles of 250 and 1,000 tablets, also in 6-oz. bottles of powder.

Please enclose professional card when requesting samples of Mead Johnson products to co-operate in preventing their reaching unauthorized persons

Mead Johnson & Company, Evansville, Indiana, U.S.A.

THESE NAMES, THESE YEARS HAVE HELPED MAKE MODERN MEDICAL HISTORY

One of a series of advertisements commemorating three-quarters of a century of progress and achievement


1879 Neisser discovers the gonococcus.
Max Nitze introduces cystoscopy.
Billings and Fletcher start *Index Medicus*.
Parke, Davis & Company introduces chemical standardization of drug extracts.
1866 1941
SEVENTY-FIVE YEARS OF SERVICE TO MEDICINE AND PHARMACY
PARKE, DAVIS & COMPANY
PIONEERS IN RESEARCH ON MEDICINAL PRODUCTS

ORY
tisements
ters of a
ievement